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TRANSMITTAL LETTER TO THE UNITED STATES

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DESIGNATED/ELECTED OFFICE (DO/EO/US)

U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR

CONCERNING A FILING UNDER 35 U.S.C. 371

09/254760

INTERNATIONAL APPLICATION NO.

INTERNATIONAL FILING DATE

PRIORITY DATE CLAIMED

PCT/JP97/03239

12 September 1997

13 September 1996

TITLE OF INVENTION

HUMAN PROTEINS HAVING SECRETORY SIGNAL SEQUENCES AND DNAs ENCODING THESE PROTEINS

APPLICANT(S) FOR DO/EO/US

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Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c) (2))
 - a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☒ has been transmitted by the International Bureau.
 - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
- ☐ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
- ☒ A copy of the International Search Report (PCT/ISA/210).
- ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
 - a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☐ have been transmitted by the International Bureau.
 - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
 - d. ☒ have not been made and will not be made.
- ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
- ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
- ☒ A copy of the International Preliminary Examination Report (PCT/IPEA/409).
- ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).

Items 13 to 18 below concern document(s) or information included:

13. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
14. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
15. ☐ A **FIRST** preliminary amendment.
A **SECOND** or **SUBSEQUENT** preliminary amendment.
16. ☐ A substitute specification.
17. ☐ A change of power of attorney and/or address letter.
18. ☒ Certificate of Mailing by Express Mail
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| U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR | | INTERNATIONAL APPLICATION NO. PCT/JP97/03239 | | ATTORNEY'S DOCKET NUMBER GI 6704PCT-US | |
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20. The following fees are submitted:.

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :

☐ Search Report has been prepared by the EPO or JPO \$930.00

☐ International preliminary examination fee paid to USPTO (37 CFR 1.482) \$720.00

☐ No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) \$790.00

☒ Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO \$1,070.00

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SEND ALL CORRESPONDENCE TO:

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 GENETICS INSTITUTE, INC.
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 SIGNATURE

Suzanne A. Sprunger, Ph.D., Esq.

 NAME

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DESCRIPTION

Human Proteins Having SecretorySignal Sequences and DNAs Encoding These Proteins

TECHNICAL FIELD

The present invention relates to human proteins having secretory signal sequences and DNAs encoding these proteins. The proteins of the present invention can be used as pharmaceuticals or as antigens for preparing antibodies against said proteins. The cDNAs of the present invention can be used as probes for the gene diagnosis and gene sources for the gene therapy. Furthermore, the cDNAs can be used as gene sources for large-scale production of the proteins encoded by said cDNAs.

BACKGROUND ART

Cells secrete many proteins outside the cells. These secretory proteins play important roles for the proliferation control, the differentiation induction, the material transportation, the biological protection, etc. in the cells. Different from intracellular proteins, the secretory proteins exert their actions outside the cells, whereby they can be administered in the intracorporeal manner such as the injection or the drip to anticipate the potentialities as medicines. In fact, a number of human secretory proteins such as interleukins, interferons, erythropoietin, thrombolytic agents, etc. have been currently utilized as

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medicines. In addition, secretory proteins other than those described above have been undergoing clinical trials to develop as pharmaceuticals. Since it has been conceived that the human cells still produce many unknown secretory proteins, availability of these secretory proteins as well as genes encoding them is expected to lead to the development of novel pharmaceuticals using these proteins.

Heretofore, such a secretory protein has been obtained by a method comprising the isolation and purification of the target protein from a large amount of the blood or a cell culture supernatant by using the biological activity as an indicator, determination of its primary structure followed by cloning of the corresponding cDNA on the basis of the information on the thus-obtained amino acid sequence, and production of the recombinant protein using said cDNA. However, the contents of the secretory proteins are generally so low that the isolation and purification are difficult in many cases. On the other hand, secretory proteins and type-I membrane proteins possess hydrophobic sequences, defined as the secretory signal sequences, consisting of about 20 amino acid residues at the amino acid termini (the N-termini). Therefore, the cloning of genes encoding the secretory proteins or type-I membrane proteins is expected to be performed by using the presence or the absence of these secretory signal sequences as indicators.

DISCLOSURE OF INVENTION

The object of the present invention is to provide novel human proteins having secretory signal sequences and DNAs

encoding said proteins.

As the result of intensive studies, the present inventors were successful in cloning of cDNAs having secretory signal sequences from a human full-length cDNA bank, thereby completing the present invention. That is to say, the present invention provides proteins containing any of the amino acid sequences represented by Sequence No. 1 to Sequence No. 9 that are human proteins having secretory signal sequences. The present invention, also, provides DNAs encoding said proteins exemplified as cDNAs containing any of the base sequences represented by Sequence No. 10 to sequence No. 18.

Each of the proteins of the present invention can be obtained, for example, by a method for isolation from human organs, cell lines, etc, a method for preparation of the peptide by the chemical synthesis on the basis of the amino acid sequence of the present invention, or a method for production with the recombinant DNA technology using the DNA encoding the human secretory protein of the present invention, wherein the method for obtainment by the recombinant DNA technology is employed preferably. For example, an in vitro expression can be achieved by preparation of an RNA by the in vitro transcription from a vector having a cDNA of the present invention, followed by the in vitro translation using this RNA as a template. Also, the recombination of the translation domain to a suitable expression vector by the method known in the art leads to the expression of a large amount of the encoded protein by using *Escherichia coli*, *Bacillus subtilis*, yeasts, animal cells, and so on.

In the case in which a protein of the present invention is expressed by a microorganism such as *Escherichia coli*, the translation region of a cDNA of the present invention is constructed in an expression vector having an origin, a promoter, ribosome-binding site(s), cDNA-cloning site(s), a terminator, etc. that can be replicated in the microorganism and, after transformation of the host cells with said expression vector, the thus-obtained transformant is incubated, whereby the protein encoded by said cDNA can be produced on a large scale in the microorganism. In that case, a maturation protein can be obtained by performing the expression with inserting an initiation codon in the translation region where the secretory signal sequence is removed. Alternatively, a fusion protein with another protein can be expressed. Only a protein portion encoding said cDNA can be obtained by cleavage of said fusion protein with an appropriate protease.

In the case in which a protein of the present invention is secretory-expressed in animal cells, the protein of the present invention can be secretory-produced as a maturation protein outside the cells, when the translation region of said cDNA is subjected to recombination to an expression vector for animal cells that has a promoter for the animal cells, a splicing domain, a poly(A) addition site, etc., followed by transfection into the animal cells.

The proteins of the present invention include peptide fragments (more than 5 amino acid residues) containing any partial amino acid sequence of the amino acid sequences represented by Sequence No. 1 to Sequence No. 9. These

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fragments can be used as antigens for preparation of the antibodies. Also, the proteins of the present invention are secreted in the form of maturation proteins outside the cells, after the signal sequences are removed. Therefore, these maturation proteins shall come within the scope of the present invention. The N-terminal amino acid sequences of the maturation proteins can be easily identified by using the method for the cleavage-site determination in a signal sequence [Japanese Patent Kokai Publication No. 1996-187100]. Furthermore, many secretory proteins are subjected to the processing after the secretion to be converted to the active forms. These activated proteins or peptides shall come within the scope of the present invention. When glycosylation sites are present in the amino acid sequences, expression in appropriate animal cells affords glycosylated proteins. Therefore, these glycosylated proteins or peptides also shall come within the scope of the present invention.

The DNAs of the present invention include all DNAs encoding the above-mentioned proteins. Said DNAs can be obtained using the method by chemical synthesis, the method by cDNA cloning, and so on.

Each of the cDNAs of the present invention can be cloned from, for example, a cDNA library of the human cell origin. The cDNA is synthesized using as a template a poly(A)⁺ RNA extracted from human cells. The human cells may be cells delivered from the human body, for example, by the operation or may be the culture cells. The cDNA can be synthesized by using any method selected from the Okayama-Berg method [Okayama, H. and Berg, P., Mol. Cell. Biol. 2: 161-170

(1982)], the Gubler-Hoffman method [Gubler, U. and Hoffman, J. Gene 25: 263-269 (1983)], and so on, but it is preferred to use the capping method [Kato, S. et al., Gene 150: 243-250 (1994)] as illustrated in Examples in order to obtain a full-length clone in an effective manner.

The primary selection of a cDNA encoding a human protein having a secretory signal sequence is performed by the sequencing of a partial base sequence of the cDNA clone selected at random from the cDNA library, sequencing of the amino acid sequence encoded by the base sequence, and recognition of the presence or absence of hydrophobic site(s) in the resulting N-terminal amino acid sequence region. Next, the secondary selection is carried out by determination of the whole base sequence by the sequencing and the protein expression by the in vitro translation. The ascertainment of the cDNA of the present invention for encoding the protein having the secretory signal sequence is performed by using the signal sequence detection method [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)]. In other words, the ascertainment for the coding portion of the inserted cDNA fragment to function as a signal sequence is provided by fusing a cDNA fragment encoding the N-terminus of the target protein with a cDNA encoding the protease domain of urokinase and then expressing the resulting cDNA in COS7 cells to detect the urokinase activity in the cell culture medium.

The cDNAs of the present invention are characterized by containing any of the base sequences represented by Sequence No. 10 to Sequence No. 18 or any of the base sequences represented by Sequence No. 19 to Sequence No. 27. Table 1

summarizes the clone number (HP number), the cells affording the cDNA, the total base number of the cDNA, and the number of the amino acid residues of the encoded protein, for each of the cDNAs.

Table 1

| Sequence Number | HP Number | Cells | Number of Bases | Number of Amino Acid Residues |
|-----------------|-----------|----------------|-----------------|-------------------------------|
| 1. 10. 19 | HP00658 | HT-1080 | 1296 | 154 |
| 2. 11. 20 | HP00714 | KB | 3311 | 315 |
| 3. 12. 21 | HP00876 | Stomach cancer | 1152 | 158 |
| 4. 13. 22 | HP01134 | Liver | 1749 | 376 |
| 5. 14. 23 | HP10029 | KB | 988 | 173 |
| 6. 15. 24 | HP10189 | KB | 390 | 93 |
| 7. 16. 25 | HP10269 | U937 | 4667 | 1172 |
| 8. 17. 26 | HP10298 | Stomach cancer | 1086 | 122 |
| 9. 18. 27 | HP10368 | Stomach cancer | 866 | 175 |

Hereupon, the same clone as any of the cDNAs of the present invention can be easily obtained by screening of the cDNA library constructed from the cell line or the human tissue employed in the present invention, by the use of an oligonucleotide probe synthesized on the basis of the corresponding cDNA base sequence depicted in Sequence No. 19 to Sequence No. 27.

In general, the polymorphism due to the individual difference is frequently observed in human genes. Therefore, any cDNA that is subjected to insertion or deletion of one or

plural nucleotides and/or substitution with other nucleotides in Sequence No. 10 to Sequence No. 27 shall come within the scope of the present invention.

In a similar manner, any protein that is produced by these modifications comprising insertion or deletion of one or plural nucleotides and/or substitution with other nucleotides shall come within the scope of the present invention, as far as said protein possesses the activity of the corresponding protein having the amino acid sequence represented by Sequence No. 1 to Sequence No. 9.

The cDNAs of the present invention include cDNA fragments (more than 10 bp) containing any partial base sequence of the base sequence represented by Sequence No. 10 to No. 18 or of the base sequence represented by Sequence No. 19 to No. 27. For example, as illustrated in Examples, the portion encoding the secretory signal sequence can be employed as means to secrete an optionally selected protein outside the cells by fusing with a cDNA encoding another protein. Also, DNA fragments consisting of a sense chain and an anti-sense chain shall come within this scope. These DNA fragments can be used as the probes for the gene diagnosis.

BRIEF DESCRIPTION OF DRAWINGS

Figure 1: A figure depicting the structure of the secretory signal sequence detection vector pSSD3.

Figure 2: A figure depicting the construction of the secretory signal sequence - the urokinase fusion gene.

Figure 3: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded

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by clone HP00685.

Figure 4: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP00714.

Figure 5: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP00876.

Figure 6: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01134.

Figure 7: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10029.

Figure 8: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10189.

Figure 9: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10269.

Figure 10: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10298.

Figure 11: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10368.

BEST MODE FOR CARRING OUT INVENTION

EXAMPLE

The present invention is embodied in more detail by the

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following examples, but this embodiment is not intended to restrict the present invention. The basic operations and the enzyme reactions with regard to the DNA recombination are carried out according to the literature ["Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory, 1989]. Unless otherwise stated, restrictive enzymes and a variety of modification enzymes to be used were those available from Takara Shuzo Co., Ltd. The manufacturer's instructions were used for the buffer compositions as well as for the reaction conditions, in each of the enzyme reactions. The cDNA synthesis was carried out according to the literature [Kato, S. et al., Gene 150: 243-250 (1994)].

(1) Preparation of Poly(A)⁺ RNA

The fibrosarcoma cell line HT-1080 (ATCC CCL 121), the epidermoid carcinoma cell line KB (ATCC CRL 17), the histiocyte lymphoma cell line U937 (ATCC CRL 1593) stimulated by phorbol esters, tissues of stomach cancer delivered by the operation, and liver were used for human cells to extract mRNAs. Each of the cell lines was cultured by a conventional procedure.

After about 1 g of human tissues was homogenized in 20 ml of a 5.5 M guanidinium thiocyanate solution, total mRNAs were prepared in accordance with the literature [Okayama, H. et al., "Methods in Enzymology" Vol. 164, Academic Press, 1987]. These mRNAs were subjected to chromatography using an oligo(dT)-cellulose column washed with 20 mM Tris-hydrochloric acid buffer solution (pH 7.6), 0.5 M NaCl, and 1 mM EDTA to obtain a poly(A)⁺ RNA in accordance with the above-mentioned literature.

(2) Construction of cDNA Library

To a solution of 10 µg of the above-mentioned poly(A)⁺ RNA in 100 mM Tris-hydrochloric acid buffer solution (pH 8) was added one unit of an RNase-free, bacterium-origin alkaline phosphatase and the resulting solution was allowed to react at 37°C for one hour. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the obtained pellets were dissolved in a mixed solution of 50 mM sodium acetate (pH 6), 1 mM EDTA, 0.1% 2-mercaptoethanol, and 0.01% Triton X-100. Thereto was added one unit of a tobacco-origin pyrophosphatase (Epicenter Technologies) and the resulting solution at a total volume of 100 µl was allowed to react at 37°C for one hour. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the thus-obtained pellets were dissolved in water to obtain a decapped poly(A)⁺ RNA solution.

To a solution of the decapped poly(A)⁺ RNA and 3 nmol of a DNA-RNA chimeric oligonucleotide (5'-dG-dG-dG-dG-dA-dA-dT-dT-dC-dG-dA-G-G-A-3') in a mixed aqueous solution of 50 mM Tris-hydrochloric acid buffer solution (pH 7.5), 0.5 mM ATP, 5 mM MgCl₂, 10 mM 2-mercaptoethanol, and 25% polyethylene glycol were added 50 units of T4 RNA ligase and the resulting solution at a total volume of 30 µl was allowed to react at 20°C for 12 hours. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the thus-obtained pellets were dissolved in water to obtain a chimeric oligo-capped poly(A)⁺ RNA.

After the vector pKA1 developed by the present inventors (Japanese Patent Kokai Publication No. 1992-117292) was digested with KpnI, an about 60-dT tail was inserted by a terminal transferase. This product was digested with EcoRV to remove the dT tail at one side and the resulting molecule was used as a vectorial primer.

After 6 μ g of the previously-prepared chimeric oligo-capped poly(A)⁺ RNA was annealed with 1.2 μ g of the vectorial primer, the product was dissolved in a mixed solution of 50 mM Tris-hydrochloric acid buffer solution (pH 8.3), 75 mM KCl, 3 mM MgCl₂, 10 mM dithiothreitol, and 1.25 mM dNTP (dATP + dCTP + dGTP + dTTP), mixed with 200 units of a reverse transferase (GIBCO-BRL), and the resulting solution at a total volume of 20 μ l was allowed to react at 42°C for one hour. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the thus-obtained pellets were dissolved in a mixed solution of 50 mM Tris-hydrochloric acid buffer solution (pH 7.5), 100 mM NaCl, 10 mM MgCl₂, and 1 mM dithiothreitol. Thereto were added 100 units of EcoRI and the resulting solution at a total volume of 20 μ l was allowed to react at 37°C for one hour. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the obtained pellets were dissolved in a mixed solution of 20 mM Tris-hydrochloric acid buffer solution (pH 7.5), 100 mM KCl, 4 mM MgCl₂, 10 mM (NH₄)₂SO₄, and 50 μ g/ml bovine serum albumin. Thereto were added 60 units of *Escherichia coli* DNA ligase and the resulting solution was allowed to react at 16°C for 16 hours.

To the reaction solution were added 2 μ l of 2 mM dNTP, 4 units of *Escherichia coli* DNA polymerase I, and 0.1 unit of *Escherichia coli* DNase H and the resulting solution was allowed to react at 12°C for one hour and then at 22°C for one hour.

Next, the cDNA-synthesis reaction solution was used to transform *Escherichia coli* DH12S (GIBCO-BRL). The transformation was carried out by the electroporation method. A portion of the transformant was inoculated on a 2xYT agar culture medium containing 100 μ g/ml ampicillin, which was incubated at 37°C overnight. A colony grown on the culture medium was randomly picked up and inoculated on 2 ml of the 2xYT culture medium containing 100 μ g/ml ampicillin, which was incubated at 37°C overnight. The culture medium was centrifuged to separate the cells, from which a plasmid DNA was prepared by the alkaline lysis method. After the plasmid DNA was double-digested with EcoRI and NotI, the product was subjected to 0.8% agarose gel electrophoresis to determine the size of the cDNA insert. In addition, by the use of the obtained plasmid as a template, the sequence reaction using M13 universal primer labeled with a fluorescent dye and Taq polymerase (a kit of Applied Biosystems Inc.) was carried out and the product was analyzed by a fluorescent DNA-sequencer (Applied Biosystems Inc.) to determine the base sequence of the cDNA 5'-terminal of about 400 bp. The sequence data were filed as a homo-protein cDNA bank data base.

(3) Selection of cDNAs Encoding Proteins Having Secretory Signal Sequence

The base sequence registered in the homo-protein cDNA

bank was converted to three frames of amino acid sequences and the presence or absence of an open reading frame (ORF) beginning from the initiation codon. Then, the selection was made for the presence of a signal sequence that is characteristic to a secretory protein at the N-terminal of the portion encoded by ORF. These clones were sequenced from the both 5' and 3' directions by using the deletion method to determine the whole base sequence. The hydrophobicity/hydrophilicity profiles were obtained for proteins encoded by ORF by the Kyte-Doolittle method [Kyte, J. & Doolittle, R. F., J. Mol. Bio. 157: 105-132 (1982)] to examine the presence or absence of a hydrophobic region. In the case in which there is not a hydrophobic region of putative transmembrane domain(s) in the amino acid sequence of an encoded protein, this protein was considered as a membrane protein that did not possess a secretory protein or transmembrane domain(s).

(4) Construction of Secretory Signal Detection Vector pSSD3

One microgram of pSSD1 carrying the SV40 promoter and a cDNA encoding the protease domain of urokinase [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)] was digested with 5 units of BglII and 5 units of EcoRV. Then, after dephosphorylation at the 5' terminal by the CIP treatment, a DNA fragment of about 4.2 kbp was purified by cutting off from the gel of agarose gel electrophoresis.

Two oligo DNA linkers, L1 (5'-GATCCCGGGTCACGTGGGAT-3') and L2 (5'-ATCCACGTGACCCGG-3'), were synthesized and phosphorylated by T4 polynucleotide kinase. After annealing

of the both linkers, followed by ligation with the previously-prepared pSSD1 fragment by T4 DNA ligase, *Escherichia coli* JM109 was transformed. A plasmid pSSD3 was prepared from the transformant and the objective recombinant was confirmed by the determination of the base sequence of the linker-inserted fragment. Figure 1 illustrates the structure of the thus-obtained plasmid. The present plasmid vector carries three types of blunt-end formation restriction enzyme sites, SmaI, PmaCI, and EcoRV. Since these cleavage sites are positioned in succession at an interval of 7 bp, selection of an appropriate site in combination of three types of frames for the inserting cDNA allows to construct a vector expressing a fusion protein.

(5) Functional Verification of Secretory Signal Sequence

Whether the N-terminal hydrophobic region in the secretory protein clone candidate obtained in the above-mentioned steps functions as the secretory signal sequence was verified by the method described in the literature [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)]. First, the plasmid containing the target cDNA was cleaved at an appropriate restriction enzyme site that existed at the downstream from the portion expected for encoding the secretory signal sequence. In the case in which this restriction enzyme site was a protruding 5'-terminus, the site was blunt-ended by the Klenow treatment. Digestion with HindIII was further carried out and a DNA fragment containing the SV40 promoter and a cDNA encoding the secretory sequence at the downstream from the promoter was separated by agarose gel electrophoresis. This fragment was inserted between the

pSSD3 HindIII site and a restriction enzyme site selected so as to match with the urokinase-coding frame, thereby constructing a vector expressing a fusion protein of the secretory signal portion of the target cDNA and the urokinase protease domain (refer to Figure 2).

After *Escherichia coli* (host: JM109) bearing the fusion-protein expression vector was incubated at 37°C for 2 hours in 2 ml of the 2xYT culture medium containing 100 µg/ml ampicillin, the helper phage M13KO7 (50 µl) was added and the incubation was continued at 37°C overnight. A supernatant separated by centrifugation underwent precipitation with polyethylene glycol to obtain single-stranded phage particles. These particles were suspended in 100 µl of 1 mM Tris-0.1 mM EDTA, pH 8 (TE). Also, there was used as a control a suspension of single-stranded particles prepared in the same manner from the vector pKA1-UPA containing pSSD3 and a full-length cDNA of urokinase [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)].

The simian-kidney-origin culture cells, COS7, were incubated at 37°C in the presence of 5% CO₂ in the Dulbecco's modified Eagle's culture medium (DMEM) containing 10% fetal calf albumin. Into a 6-well plate (Nunc Inc., 3 cm in the well diameter) were inoculated 1×10^5 COS7 cells and incubation was carried out at 37°C for 22 hours in the presence of 5% CO₂. After the culture medium was removed, the cell surface was washed with a phosphate buffer solution and then washed again with DMEM containing 50 mM Tris-hydrochloric acid (pH 7.5) (TDMEM). To the cells were added 1 µl of the single-stranded phage suspension, 0.6 ml of the

DMEM culture medium, and 3 μ l of TRANSFECTAMTM (IBF Inc.) and the resulting mixture was incubated at 37°C for 3 hours in the presence of 5% CO₂. After the sample solution was removed, the cell surface was washed with TDMEM, 2 ml per well of DMEM containing 10% fetal calf albumin was added, and the incubation was carried out at 37°C for 2 days in the presence of 5% CO₂.

To 10 ml of 50 mM phosphate buffer solution (pH 7.4) containing 2% bovine fibrinogen (Miles Inc.), 0.5% agarose, and 1 mM potassium chloride were added 10 units of human thrombin (Mochida Pharmaceutical Co., Ltd.) and the resulting mixture was solidified in a plate of 9 cm in diameter to prepare a fibrin plate. Ten microliters of the culture supernatant of the transfected COS7 cells were spotted on the fibrin plate, which was incubated at 37°C for 15 hours. The diameter of the thus-obtained clear circle was taken as an index for the urokinase activity. Table 2 shows the restriction enzyme site used for cutting off the cDNA fragment from each clone, the restriction enzyme site used for cleavage of pSSD3, and the presence or absence of a clear circle. Except for pSSD3 used as the control, each of the samples formed a clear circle to identify that urokinase was secreted in the culture medium. That is to say, it is indicated that each of the cDNA fragments codes for the amino acid sequence that functions as the secretory signal sequence.

Table 2

| HP Number | Restriction Enzyme Site | | Clear Circle |
|-----------|-------------------------|--------|--------------|
| | cDNA* | Vector | |
| HP00658 | HindIII (K) | SmaI | + |
| HP00714 | PvuII | PmaCI | + |
| HP00876 | NcoI (K) | PmaCI | + |
| HP01134 | PmaCI | PmaCI | + |
| HP10029 | ApaI (K) | SmaI | + |
| HP10189 | BglI (K) | PmaCI | + |
| HP10269 | PvuII | PmaCI | + |
| HP10298 | HindIII (K) | PmaCI | + |
| HP10368 | EcoRV | PmaCI | + |
| pKA1-UPA | | | + |
| pSSD3 | | | - |

* (K) means that cleavage with the restriction enzyme is followed by the Klenow treatment.

(6) Protein Synthesis by In Vitro Translation

The plasmid vector carrying the cDNA of the present invention was utilized for the in vitro transcription/translation by the T_NT rabbit reticulocyte lysate kit (Promega Biotec). In this case, [³⁵S]methionine was added and the expression product was labeled with the radioisotope. All reactions were carried out by following the protocols attached to the kit. Two micrograms of the plasmid was allowed to react at 30°C for 90 minutes in total 25 ml of a reaction solution containing 12.5 µl of the T_NT rabbit reticulocyte lysate, 0.5 µl of the buffer solution (attached to the kit), 2 µl of an amino acid mixture (methionine-free),

2 μ l (0.37 MBq/ μ l) of [35 S]methionine (Amersham Corporation), 0.5 μ l of T7 RNA polymerase, and 20 U of RNasin. Also, the experiment in the presence of the membrane system was carried out by adding 2.5 μ l of the dog pancreatic microsome fraction (Promega Biotec) into this reaction system. To 3 μ l of the reaction solution was added 2 μ l of an SDS sampling buffer (125 mM Tris-hydrochloric acid buffer solution, pH 6.8, 120 mM 2-mercaptoethanol, 2% SDS solution, 0.025% bromophenol blue, and 20% glycerol) and the resulting solution was heated at 95°C for 3 minutes and then subjected to SDS-polyacrylamide gel electrophoresis. The molecular weight of the translation product was determined by carrying out the autoradiography. Table 3 shows the molecular weight of the in vitro translation product obtained from each of the clones in the presence/absence of the membrane microsome together with the calculated value of the molecular weight of the protein encoded by ORF of the cDNA.

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| | |
|----------|---|
| | 1 |
| umber 1, | |
| whole b | |

| | | | | |
|---|---------|---------|-----|----|
| 6 | HP10189 | 9,113 | 12 | - |
| 7 | HP10269 | 129,572 | 130 | - |
| 8 | HP10298 | 13,161 | 16 | - |
| 9 | HP10368 | 19,979 | 19 | 18 |

* - means "Not examined".

(7) Clone Examples

<HP00658> (Sequence Number 1, 10, 19)

Determination of the whole base sequence for the cDNA

| | | |
|---|---------|--------|
| 6 | HP10189 | 9,11 |
| 7 | HP10269 | 129,57 |
| 8 | HP10298 | 13,16 |
| 9 | HP10368 | 19,97 |

* - means "Not examined".

(7) Clone Examples

<HP00658> (Sequence M

Determination of the

| | |
|---------|-----|
| HP10189 | 9 |
| HP10269 | 129 |
| HP10298 | 13 |
| HP10368 | 19 |

means "Not examine

(7) Clone Examples

<HP00658> (Sequenc

Determination of t

| | | |
|---------|---------|-----|
| HP10189 | 9,113 | 12 |
| HP10269 | 129,572 | 130 |
| HP10298 | 13,161 | 16 |
| HP10368 | 19,979 | 19 |

means "Not examined".

(7) Clone Examples

<HP00658> (Sequence Number 1, 10, 19)

Determination of the whole base sequence of the clone HP00658 is shown in Figure 1.

| | | | | |
|---|---------|---------|-----|----|
| 6 | HP10189 | 9,113 | 12 | - |
| 7 | HP10269 | 129,572 | 130 | - |
| 8 | HP10298 | 13,161 | 16 | - |
| 9 | HP10368 | 19,979 | 19 | 18 |

* - means "Not examined".

(7) Clone Examples

<HP00658> (Sequence Number 1, 10, 19)

Determination of the whole base sequence for the cDNA

revealed that the N-terminal 63 amino acid residues thereof were completely identical with those in the RANTES protein (EMBL Accession No. 21121) except for one amino acid residue at position 7 (arginine in RANTES and alanine in the present protein), but the sequences in both proteins were completely different after position 64. Hereupon, RANTES consisted of 91 amino acid residues, whereas the present protein consisted of longer 154 amino acid residues. The in vitro translation resulted in the formation of a translation product of 18 kDa that was almost consistent with the molecular weight of 17,037 predicted from the ORF. In this case, the addition of the microsome resulted in the formation of a 16-kDa product in which the secretory signal sequence portion was putatively removed by cleavage. This result together with the result on pSSD3 verifies that the present protein possesses the secretory signal sequence. Application of the (-3,-1) rule, a method for predicting the signal sequence cleavage site [von Heijne, G., Nucl. Acid Res. 14: 4683-4690 (1986)], allows to expect that the maturation protein starts from serine at position 24.

Comparison of the base sequences for the both proteins revealed that the base sequence from position 2 to position 325 in the present cDNA was deficient in the RANTES cDNA. It is considered that this deficiency resulted in induction of a frame shift to form an ORF of a different size. Some mutations were observed in other regions, wherein the homology was 97.7% up to position 241 and was 98.0% after position 325. RANTES has been obtained as a T cell-specific protein [Schall, T. J. et al., J. Immunol. 141: 1018-1025

(1988)], whereas the present cDNA was obtained from the fibrosarcoma cells. Accordingly, the present protein is considered to possess a different function from that of RANTES.

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that any EST possessing the homology of 90% or more was not found.

<HP00714> (Sequence Number 2, 11, 20)

Determination of the whole base sequence for the cDNA insert of clone HP00714 obtained from the human epidermoid carcinoma cell line KB cDNA libraries revealed the structure consisting of a 5'-non-translation region of 56 bp, an ORF of 948 bp, and a 3'-non-translation region of 2310 bp. The ORF codes for a protein consisting of 315 amino acid residues with a hydrophobic region of a putative secretory signal sequence at the N-terminal. Figure 4 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 47 kDa that was somewhat larger than the molecular weight of 37,106 predicted from the ORF. Since the molecular weight of the human reticulocalbin analogous to the present protein is also larger by about 10 kDa than the molecular weight expected from the translation-product band on SDS-PAGE [Ozawa, M., J. Biochem. 117: 1113-1119 (1995)], the molecular weight difference in the present protein is considered to be arisen from its physicochemical properties. Application of the (-3,-1) rule, a method for predicting the signal sequence cleavage site, allows to expect that the maturation protein

starts from lysine at position 20. There is a possibility that the present protein exists in the endoplasmic reticulum because this protein possesses the C-terminal sequence HDEF analogous to KDEL, the signal motif sequence localized in the endoplasmic reticulum.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the human reticulocalbin (GenBank Accession No. D42073). Table 4 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the human reticulocalbin (RC). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 60.5%.

Table 4

| | |
|----|---|
| HP | MDLRQFLMCLSLCTAFALSKPTEKKDR-VHHEPQLSDKVHNDQAQSFQYDH |
| | . * . * * . . * * * . * * * . . . * . . . * . * * * . * * * |
| RC | MARGGRGRRGLGLALLLALVLAAPRVLRAKPTVRKERVVRPDSELGERPPEDNQSFQYDH |
| HP | DAFLGAEEAKTFDQLTPESKERLGKIVSKI DGDGDFVTVDLKDWDIKFAQKRWIYEDV |
| | . * * * * * . . * * * * * * . * * * * * * . * * . * * * . * * * . * * * . * * * |
| RC | EAFLGKEDSKTFDQLTPDESKERLGKIVDRIDNDGDFVTTEELKTWIKRVQKRYIFDNV |
| HP | ERQWKGHDLNEDGLVSWEEYKNATYGYVLDDP-----DPDDGFNYKQMMVRDERRFKMADK |
| | . . * * . * . . * . * * * * * . * * * * * . * . * . . * . * . * * * * * * |
| RC | AKVWKDYDRDKDDKISWEEYKQATYGYLGNPAEFHDSSDHHTFKKMLPRDERRFKAADL |
| HP | DGDLIATKEEFTAFLLHPEEYDYMKDIVVQETMEDIDKNADGFIDLEEYIGDMYSHDGNTD |

. ***. **. *****... **. *** **. *****. ***. * . ***. **. **. *.
 RC NGDLTATREEFTAFLLHPEEFHEMKEIVVLETLEDIDKNGDGFVDQDEYIADMFSHEENGP
 HP EPEWVKTEREQFVEFRDKNRDGKMDKEETKDWILPSDYDHAEAEARHLVYESDQNKDGKL
 . ** . *** **** *. ***. **. *. ... ***** *****, *****, *****, **. **
 RC EPDWVLSEREQFNEFRDLNKDGKLDKDEIRHWILPQDYDHAQAEARHLVYESDKNKDEKL
 HP TKEEIVDKYDLFVGSQATDFGEALVR-HDEF
 *****..... *****.. **. *. . ***.
 RC TKEEILENWNMFVGSQATNYGEDLTKNHDEL

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more and containing the initiation codon (for example, Accession No. F3872), but any of the sequences thereof did not allow to predict the present protein.

Reticulocalbin is a protein localized on the membrane surface of the endoplasmic reticulum and has been considered to participate in the protein folding. Accordingly, the protein of the present invention is considered to be applicable to the folding process of recombinant proteins.

<HP00876> (Sequence Number 3, 12, 21)

Determination of the whole base sequence for the cDNA insert of clone HP0876 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 146 bp, an ORF of 477 bp, and a 3'-non-translation region of 529 bp. The ORF codes for a protein consisting of 158 amino acid residues with a hydrophobic region of a putative secretory signal sequence at the N-terminal. Figure 5 depicts the hydrophobicity/hydrophilicity

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profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 18 kDa that was almost consistent with the molecular weight of 18,230 predicted from the ORF. In this case, the addition of the microsome resulted in the formation of a 16-kDa product in which the secretory signal sequence portion was putatively removed by cleavage. This result together with the result on pSSD3 verifies that the present protein possesses the secretory signal. Application of the (-3,-1) rule, a method for predicting the signal sequence cleavage site, allows to expect that the maturation protein starts from glycine at position 18 or aspartic acid at position 23.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to several type-C lectins. As an example, Table 5 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the rattlesnake lectin (CL) (Swiss-PROT Accession No. P21963). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 35.3%.

HP MASRSMRLLLLLSCLAKTGVLGDIIMRPSCAPGWFYHKSNCYGYFRKLNRNWSDAELECQS
 .*. *. .. ** *. *. *. ***. *.
 CL NNCPLDWLPMNGLCYKIFNQLKTWEDAEMFCRK
 HP YGNGAHLASILSLKEASTIABYISGYQRSQ-PIWIGLHDPQKRQQWQWIDGAMYLYRSWS
 * * ****. . *. *****. *. . * . ****. * . * * . * . * .
 CL YKPGCHLASFHRYGESLEIABYISDYHKGQENVWIGLRDKKKDFSWEWTD RSCTDYLTWD
 HP GKSMGG--NKH-CAEMSSNNNFLTWSSNECNKRQHFLCKYRP
 . . **. *. * * ... *... *... ***...
 CL KNQPDHYQNKEFCVELVSLTGYRLWNDQVCESKDAFLCQCKF

After 1 μ g of the plasmid pHP00876 was digested with 20 units of PvuII, the product was subjected to 1% agarose gel electrophoresis and an about 700-bp DNA fragment was cut off from the gel. Next, 1 μ g of pET-21a (Novagen) was digested with 20 units of NheI, the product was subjected to the Klenow treatment followed by 1% agarose gel electrophoresis and an about 5.4-kbp DNA fragment was cut off from the gel. After ligation of the vector fragment and the cDNA fragment using a ligation kit, *Escherichia coli* BL21 (DE3) (Novagen) was transformed. A plasmid pET876 was prepared from the transformant and the objective recombinant was confirmed from the restriction enzyme cleavage map. The present expression vector expresses a protein in which methionine-alanine was

inserted before a protein starting from serine at position 29 in the protein encoded by the clone HP00876.

A suspension of pET876/BL21 (DE3) in 5 ml of the LB culture medium containing 100 µg/ml ampicillin was incubated in a shaker at 37°C and isopropylthiogalactoside was added to make 1 mM when A₆₀₀ reached to about 0.5. After the incubation was continued at 37°C for 6 hours, cells were collected by centrifugation and suspended in 25 ml of a column buffer solution for the amylose column (10 mM Tris-hydrochloric acid, pH 7.4, 200 mM NaCl, and 1 mM EDTA). The resulting suspension was sonicated and then the insoluble fraction was subjected to SDS-polyacrylamide electrophoresis to identify a band originating from the expression of the present vector at a position of about 14 kDa.

Since lectins recognize and then bind to sugar chains, lectins are useful as sugar-chain detection reagents and as affinity carriers for purification of glycoproteins. In addition, extracellular secretory lectins play important roles also in intercellular signal transduction and thereby are useful as medicines.

<HP01134> (Sequence Number 4, 13, 22)

Determination of the whole base sequence for the cDNA insert of clone HP01134 obtained from the human liver cDNA libraries revealed the structure consisting of a 5'-non-translation region of 116 bp, an ORF of 1131 bp, and a 3'-non-translation region of 502 bp. The ORF codes for a protein consisting of 376 amino acid residues with a hydrophobic region of a putative secretory signal sequence at the N-terminal. Figure 6 depicts the hydrophobicity/hydrophilicity

profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 42 kDa that was almost consistent with the molecular weight of 42,947 predicted from the ORF. In this case, the addition of the microsome resulted in the formation of a 49-kDa product in which a sugar chain was putatively added by N-glycosylation after the secretion. Hereupon, there exist in the amino acid sequence of this protein four possible N-glycosylation sites (Asn-Gly-Thr at position 91, Asn-Glu-Thr at position 167, Asn-Thr-Ser at position 263, and Asn-Lys-Thr at position 272). The above result together with the result on pSSD3 verifies that the present protein possesses the secretory signal. Application of the (-3,-1) rule, a method for predicting the signal sequence cleavage site, allows to expect that the maturation protein starts from alanine at position 17 or valine at position 18.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to several cysteine proteinases. As an example, Table 6 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the tangerine cysteine proteinase (CP) (GenBank Accession No. Z47793). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 49% among the N-terminal region of 286 amino acid residues.

| Category | Item | Value |
|----------|--------------|-------|
| General | 1. General | 100 |
| | 2. General | 100 |
| | 3. General | 100 |
| | 4. General | 100 |
| | 5. General | 100 |
| | 6. General | 100 |
| | 7. General | 100 |
| | 8. General | 100 |
| | 9. General | 100 |
| | 10. General | 100 |
| Specific | 1. Specific | 100 |
| | 2. Specific | 100 |
| | 3. Specific | 100 |
| | 4. Specific | 100 |
| | 5. Specific | 100 |
| | 6. Specific | 100 |
| | 7. Specific | 100 |
| | 8. Specific | 100 |
| | 9. Specific | 100 |
| | 10. Specific | 100 |
| Other | 1. Other | 100 |
| | 2. Other | 100 |
| | 3. Other | 100 |
| | 4. Other | 100 |
| | 5. Other | 100 |
| | 6. Other | 100 |
| | 7. Other | 100 |
| | 8. Other | 100 |
| | 9. Other | 100 |
| | 10. Other | 100 |

| Category | Item | Value |
|----------|--------------|-------|
| General | 1. General | 100 |
| | 2. General | 100 |
| | 3. General | 100 |
| | 4. General | 100 |
| | 5. General | 100 |
| | 6. General | 100 |
| | 7. General | 100 |
| | 8. General | 100 |
| | 9. General | 100 |
| | 10. General | 100 |
| Specific | 1. Specific | 100 |
| | 2. Specific | 100 |
| | 3. Specific | 100 |
| | 4. Specific | 100 |
| | 5. Specific | 100 |
| | 6. Specific | 100 |
| | 7. Specific | 100 |
| | 8. Specific | 100 |
| | 9. Specific | 100 |
| | 10. Specific | 100 |
| Other | 1. Other | 100 |
| | 2. Other | 100 |
| | 3. Other | 100 |
| | 4. Other | 100 |
| | 5. Other | 100 |
| | 6. Other | 100 |
| | 7. Other | 100 |
| | 8. Other | 100 |
| | 9. Other | 100 |
| | 10. Other | 100 |

| Category | Item | Value |
|----------|--------------|-------|
| General | 1. General | 100 |
| | 2. General | 100 |
| | 3. General | 100 |
| | 4. General | 100 |
| | 5. General | 100 |
| | 6. General | 100 |
| | 7. General | 100 |
| | 8. General | 100 |
| | 9. General | 100 |
| | 10. General | 100 |
| Specific | 1. Specific | 100 |
| | 2. Specific | 100 |
| | 3. Specific | 100 |
| | 4. Specific | 100 |
| | 5. Specific | 100 |
| | 6. Specific | 100 |
| | 7. Specific | 100 |
| | 8. Specific | 100 |
| | 9. Specific | 100 |
| | 10. Specific | 100 |
| Other | 1. Other | 100 |
| | 2. Other | 100 |
| | 3. Other | 100 |
| | 4. Other | 100 |
| | 5. Other | 100 |
| | 6. Other | 100 |
| | 7. Other | 100 |
| | 8. Other | 100 |
| | 9. Other | 100 |
| | 10. Other | 100 |

Extracellular secretory proteases possess a variety of physiological functions and thereby are useful as medicines. In addition, the proteases have been utilized as research reagents for the structure analysis of proteins by restricted degradation and so on.

<HP10029> (Sequence Number 5, 14, 23)

Determination of the whole base sequence for the cDNA insert of clone HP10029 obtained from the human epidermoid carcinoma cell line KB cDNA libraries revealed the structure consisting of a 5'-non-translation region of 8 bp, an ORF of 522 bp, and a 3'-non-translation region of 458 bp. The ORF codes for a protein consisting of 173 amino acid residues with a hydrophobic region of a putative secretory signal sequence at the N-terminal. Figure 7 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 21 kDa that was almost consistent with the molecular weight of 18,894 predicted from the ORF. In this case, the addition of the microsome resulted in the formation of a 18-kDa product in which the secretory signal sequence portion was putatively removed by cleavage. This result together with the result on pSSD3 verifies that the present protein possesses the secretory signal sequence. Application of the (-3,-1) rule, a method for predicting the signal sequence cleavage site, allows to expect that the maturation protein starts from valine at position 32. There is a possibility that the present protein exists in the endoplasmic reticulum because this protein possesses the C-

terminal sequence RTEL analogous to KDEL, the signal motif sequence localized in the endoplasmic reticulum.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not homologous with any of known proteins. Hereupon, the search of GenBank using the base sequence revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. H87021), but they were shorter than the present cDNA and any molecule containing the initiation codon was not identified.

<HP10189> (Sequence Number 6, 15, 24)

Determination of the whole base sequence for the cDNA insert of clone HP10189 obtained from the human epidermoid carcinoma cell line KB cDNA libraries revealed the structure consisting of a 5'-non-translation region of 101 bp, an ORF of 222 bp, and a 3'-non-translation region of 67 bp. The ORF codes for a protein consisting of 73 amino acid residues with a hydrophobic region of a putative secretory signal sequence at the N-terminal. Figure 8 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 10 kDa that was almost consistent with the molecular weight of 9,113 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the signal sequence cleavage site, allows to expect that the maturation protein starts from alanine at position 27.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was

not homologous with any of known proteins. Hereupon, the search of GenBank using the base sequence revealed that there existed some ESTs possessing the homology of 90% or more and containing the initiation codon (for example, Accession No. N56270), but a frame shift had occurred and the same ORF as that in the present cDNA was not identified.

<HP10269> (Sequence Number 7, 16, 25)

Determination of the whole base sequence for the cDNA insert of clone HP10269 obtained from the human lymphoma cell line U937 cDNA libraries revealed the structure consisting of a 5'-non-translation region of 753 bp, an ORF of 351 bp, and a 3'-non-translation region of 395 bp. The ORF codes for a protein consisting of 1172 amino acid residues with a hydrophobic region of a putative secretory signal sequence at the N-terminal. Figure 9 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 130 kDa that was almost consistent with the molecular weight of 129,571 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the signal sequence cleavage site, allows to expect that the maturation protein starts from glutamine at position 18.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the B3 chain of laminin S. Table 7 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the B3 chain of human laminin S (B3) (GenBank Accession No. L25541)

Table 7

| Amino Acid Residue Number | HP | B3 |
|---------------------------|-----|-----------|
| 124 | Gln | Arg |
| 269 | Pro | Deficient |
| 388 | Pro | Ala |
| 426 | Gln | Arg |
| 427 | Gly | Arg |
| 439 | Arg | Deficient |
| 441 | Asp | Glu |
| 603 | Arg | Pro |
| 815 | Gly | Ala |

Comparison of the base sequence of the present cDNA and the base sequence described in the data base reveals that the 5'-terminus in the present cDNA is longer by 600 or more bp and the 81-bp 5'-terminus in the base sequence described in the data base is not consistent at all with the base sequence of the present cDNA. Accordingly, the both proteins originate from different mRNAs.

As an extracellular matrix, laminin deeply participates in the proliferation and differentiation of cells. Accordingly, laminin has been employed as an additive for the cell culture and so on.

<HP10298> (Sequence Number 8, 17, 26)

Determination of the whole base sequence for the cDNA insert of clone HP10298 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 137 bp, an ORF of 369 bp, and a

3'-non-translation region of 580 bp. The ORF codes for a protein consisting of 122 amino acid residues with a hydrophobic region of a putative secretory signal sequence at the N-terminal. Figure 10 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 16 kDa that was almost consistent with the molecular weight of 13,161 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the signal sequence cleavage site, allows to expect that the maturation protein starts from leucine at position 18. There is also a possibility that the present protein possessing the hydrophobic C-terminal sequence of about 20 amino acid residues binds to the membrane via this portion.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not homologous with any of known proteins. Hereupon, the search of GenBank using the base sequence revealed that there existed some ESTs possessing the homology of 90% or more and containing the initiation codon (for example, Accession No. D78655), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

<HP10368> (Sequence Number 9, 18, 27)

Determination of the whole base sequence for the cDNA insert of clone HP10368 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 72 bp, an ORF of 528 bp, and a 3'-non-translation region of 266 bp. The ORF codes for a

protein consisting of 175 amino acid residues with a hydrophobic region of a putative secretory signal sequence at the N-terminal. Figure 11 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 20 kDa that was almost consistent with the molecular weight of 19,979 predicted from the ORF. In this case, the addition of the microsome resulted in the formation of a 19-kDa product in which the secretory signal sequence portion was putatively removed by cleavage. This result together with the result on pSSD3 verifies that the present protein possesses the secretory signal. Application of the (-3,-1) rule, a method for predicting the signal sequence cleavage site, allows to expect that the maturation protein starts from leucine at position 19 or arginine at position 21. There is a possibility that the present protein exists in the endoplasmic reticulum because this protein possesses the C-terminal sequence KTEL analogous to KDEL, the signal motif sequence localized in the endoplasmic reticulum.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not homologous with any of known proteins. Hereupon, the search of GenBank using the base sequence revealed that there existed some ESTs possessing the homology of 90% or more and containing the initiation codon (for example, Accession No. T86663), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

INDUSTRIAL APPLICATION

The present invention provides human proteins having secretory signal sequences and cDNAs encoding said proteins. All of the proteins of the present invention are putative proteins controlling the proliferation and differentiation of the cells, because said proteins are secreted outside the cells and exist in the extracellular liquid or on the cell membrane surface. Therefore, the proteins of the present invention can be used as pharmaceuticals or as antigens for preparing antibodies against said proteins. Furthermore, said DNAs can be used for the expression of large amounts of said proteins.

In addition to the activities and uses described above, the polynucleotides and proteins of the present invention may exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

Research Uses and Utilities

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a

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particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers

for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

Nutritional Uses

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases

the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

Cytokine and Cell Proliferation/Differentiation Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e and CMK.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays

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for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152:1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon γ , Schreiber, R.D. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6 -Nordan, R. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci.

U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 - Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

Immune Stimulating or Suppressing Activity

A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating

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(up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitus, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

Using the proteins of the invention it may also be

possible to immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural

ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine

the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor:ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythematosus in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy.

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Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid

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encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I α chain protein and β_2 microglobulin protein or an MHC class II α chain protein and an MHC class II β chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T

cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowman et al., J. Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991;

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Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology

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67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

Hematopoiesis Regulating Activity

A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in

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combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or ex-vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M.G. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R.E. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

Tissue Growth Activity

A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may

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be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon- or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be useful

for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of

cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon); International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

Activin/Inhibin Activity

A protein of the present invention may also exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of

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follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin α family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- β group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

Chemotactic/Chemokinetic Activity

A protein of the present invention may have chemotactic

or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to

another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke).

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79

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(1991); Schaub, Prostaglandins 35:467-474, 1988.

Receptor/Ligand Activity

A protein of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein

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et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

Anti-Inflammatory Activity

Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

Tumor Inhibition Activity

In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A

protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth

Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent

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which is cross-react

SEQUENCE LISTING

Sequence No.: 1

Sequence length: 154

Sequence type: Amino acid

Topology: Linear

Sequence kind: Protein

Hypothetical: No

Original source:

Organism species: *Homo sapiens*

Cell kind: Fibrosarcoma

Cell line: HT-1080

Clone name: HP00658

Sequence description

Met Lys Val Ser Ala Ala Ala Leu Ala Val Ile Leu Ile Ala Thr Ala
1 5 10 15
Leu Cys Ala Pro Ala Ser Ala Ser Pro Tyr Ser Ser Asp Thr Thr Pro
20 25 30
Cys Cys Phe Ala Tyr Ile Ala Arg Pro Leu Pro Arg Ala His Ile Lys
35 40 45
Glu Tyr Phe Tyr Thr Ser Gly Lys Cys Ser Asn Pro Ala Val Val His
50 55 60
Arg Ser Arg Met Pro Lys Arg Glu Gly Gln Gln Val Trp Gln Asp Phe
65 70 75 80
Leu Tyr Asp Ser Arg Leu Asn Lys Gly Lys Leu Cys His Pro Lys Glu
85 90 95
Pro Pro Ser Val Cys Gln Pro Arg Glu Glu Met Gly Ser Gly Val His
100 105 110
Gln Leu Phe Gly Asp Glu Leu Gly Trp Arg Val Leu Glu Pro Glu Leu

Sequence No.: 2

Sequence type: Amino acid

Sequence kind: Protein

Original source:

Cell kind: Epidermoid carcinoma

Clone name: HP00714

Met Asp Leu Arg Gln Phe Leu Met Cys Leu Ser Leu Cys Thr Ala Phe

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1             5             10             15
Ala Leu Ser Lys Pro Thr Glu Lys Lys Asp Arg Val His His Glu Pro
      20             25             30
Gln Leu Ser Asp Lys Val His Asn Asp Ala Gln Ser Phe Asp Tyr Asp
      35             40             45
His Asp Ala Phe Leu Gly Ala Glu Glu Ala Lys Thr Phe Asp Gln Leu
      50             55             60
Thr Pro Glu Glu Ser Lys Glu Arg Leu Gly Lys Ile Val Ser Lys Ile
      65             70             75             80
Asp Gly Asp Lys Asp Gly Phe Val Thr Val Asp Glu Leu Lys Asp Trp

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66
 85 90 95
 Ile Lys Phe Ala Gln Lys Arg Trp Ile Tyr Glu Asp Val Glu Arg Gln
 100 105 110
 Trp Lys Gly His Asp Leu Asn Glu Asp Gly Leu Val Ser Trp Glu Glu
 115 120 125
 Tyr Lys Asn Ala Thr Tyr Gly Tyr Val Leu Asp Asp Pro Asp Pro Asp
 130 135 140
 Asp Gly Phe Asn Tyr Lys Gln Met Met Val Arg Asp Glu Arg Arg Phe
 145 150 155 160
 Lys Met Ala Asp Lys Asp Gly Asp Leu Ile Ala Thr Lys Glu Glu Phe
 165 170 175
 Thr Ala Phe Leu His Pro Glu Glu Tyr Asp Tyr Met Lys Asp Ile Val
 180 185 190
 Val Gln Glu Thr Met Glu Asp Ile Asp Lys Asn Ala Asp Gly Phe Ile
 195 200 205
 Asp Leu Glu Glu Tyr Ile Gly Asp Met Tyr Ser His Asp Gly Asn Thr
 210 215 220
 Asp Glu Pro Glu Trp Val Lys Thr Glu Arg Glu Gln Phe Val Glu Phe
 225 230 235 240
 Arg Asp Lys Asn Arg Asp Gly Lys Met Asp Lys Glu Glu Thr Lys Asp
 245 250 255
 Trp Ile Leu Pro Ser Asp Tyr Asp His Ala Glu Ala Glu Ala Arg His
 260 265 270
 Leu Val Tyr Glu Ser Asp Gln Asn Lys Asp Gly Lys Leu Thr Lys Glu
 275 280 285
 Glu Ile Val Asp Lys Tyr Asp Leu Phe Val Gly Ser Gln Ala Thr Asp
 290 295 300
 Phe Gly Glu Ala Leu Val Arg His Asp Glu Phe
 305 310 315

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Sequence No.: 3

Sequence length: 158

Sequence type: Amino acid

Topology: Linear

Sequence kind: Protein

Hypothetical: No

Original source:

Organism species: *Homo sapiens*

Cell kind: Stomach cancer

Clone name: HP00876

Sequence description

Met Ala Ser Arg Ser Met Arg Leu Leu Leu Leu Leu Ser Cys Leu Ala
1 5 10 15
Lys Thr Gly Val Leu Gly Asp Ile Ile Met Arg Pro Ser Cys Ala Pro
20 25 30
Gly Trp Phe Tyr His Lys Ser Asn Cys Tyr Gly Tyr Phe Arg Lys Leu
35 40 45
Arg Asn Trp Ser Asp Ala Glu Leu Glu Cys Gln Ser Tyr Gly Asn Gly
50 55 60
Ala His Leu Ala Ser Ile Leu Ser Leu Lys Glu Ala Ser Thr Ile Ala
65 70 75 80
Glu Tyr Ile Ser Gly Tyr Gln Arg Ser Gln Pro Ile Trp Ile Gly Leu
85 90 95
His Asp Pro Gln Lys Arg Gln Gln Trp Gln Trp Ile Asp Gly Ala Met
100 105 110
Tyr Leu Tyr Arg Ser Trp Ser Gly Lys Ser Met Gly Gly Asn Lys His
115 120 125
Cys Ala Glu Met Ser Ser Asn Asn Asn Phe Leu Thr Trp Ser Ser Asn

68

130 135 140
 Glu Cys Asn Lys Arg Gln His Phe Leu Cys Lys Tyr Arg Pro
 145 150 155

Sequence No.: 4

Sequence length: 376

Sequence type: Amino acid

Topology: Linear

Sequence kind: Protein

Hypothetical: No

Original source:

Organism species: *Homo sapiens*

Cell kind: Liver

Clone name: HP01134

Sequence description

Met Val Trp Lys Val Ala Val Phe Leu Ser Val Ala Leu Gly Ile Gly
 1 5 10 15
 Ala Val Pro Ile Asp Asp Pro Glu Asp Gly Gly Lys His Trp Val Val
 20 25 30
 Ile Val Ala Gly Ser Asn Gly Trp Tyr Asn Tyr Arg His Gln Ala Asp
 35 40 45
 Ala Cys His Ala Tyr Gln Ile Ile His Arg Asn Gly Ile Pro Asp Glu
 50 55 60
 Gln Ile Val Val Met Met Tyr Asp Asp Ile Ala Tyr Ser Glu Asp Asn
 65 70 75 80
 Pro Thr Pro Gly Ile Val Ile Asn Arg Pro Asn Gly Thr Asp Val Tyr
 85 90 95
 Gln Gly Val Pro Lys Asp Tyr Thr Gly Glu Asp Val Thr Pro Gln Asn
 100 105 110

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Phe Leu Ala Val Leu Arg Gly Asp Ala Glu Ala Val Lys Gly Ile Gly
 115 120 125
 Ser Gly Lys Val Leu Lys Ser Gly Pro Gln Asp His Val Phe Ile Tyr
 130 135 140
 Phe Thr Asp His Gly Ser Thr Gly Ile Leu Val Phe Pro Asn Glu Asp
 145 150 155 160
 Leu His Val Lys Asp Leu Asn Glu Thr Ile His Tyr Met Tyr Lys His
 165 170 175
 Lys Met Tyr Arg Lys Met Val Phe Tyr Ile Glu Ala Cys Glu Ser Gly
 180 185 190
 Ser Met Met Asn His Leu Pro Asp Asn Ile Asn Val Tyr Ala Thr Thr
 195 200 205
 Ala Ala Asn Pro Arg Glu Ser Ser Tyr Ala Cys Tyr Tyr Asp Glu Lys
 210 215 220
 Arg Ser Thr Tyr Leu Gly Asp Trp Tyr Ser Val Asn Trp Met Glu Asp
 225 230 235 240
 Ser Asp Val Glu Asp Leu Thr Lys Glu Thr Leu His Lys Gln Tyr His
 245 250 255
 Leu Val Lys Ser His Thr Asn Thr Ser His Val Met Gln Tyr Gly Asn
 260 265 270
 Lys Thr Ile Ser Thr Met Lys Val Met Gln Phe Gln Gly Met Lys Arg
 275 280 285
 Lys Ala Ser Ser Pro Val Pro Leu Pro Pro Val Thr His Leu Asp Leu
 290 295 300
 Thr Pro Ser Pro Asp Val Pro Leu Thr Ile Met Lys Arg Lys Leu Met
 305 310 315 320
 Asn Thr Asn Asp Leu Glu Glu Ser Arg Gln Leu Thr Glu Glu Ile Gln
 325 330 335
 Arg His Leu Asp Tyr Glu Tyr Ala Leu Arg His Leu Tyr Val Leu Val

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70

340 345 350
 Asn Leu Cys Glu Lys Pro Tyr Pro Leu His Arg Ile Lys Leu Ser Met
 355 360 365
 Asp His Val Cys Leu Gly His Tyr
 370 375

Sequence No.: 5

Sequence length: 173

Sequence type: Amino acid

Topology: Linear

Sequence kind: Protein

Hypothetical: No

Original source:

Organism species: *Homo sapiens*

Cell kind: Epidermoid carcinoma

Cell line: KB

Clone name: HP10029

Sequence description

Met Ala Ala Pro Ser Gly Gly Trp Asn Gly Val Arg Ala Ser Leu Trp
 1 5 10 15
 Ala Ala Leu Leu Leu Gly Ala Val Ala Leu Arg Pro Ala Glu Ala Val
 20 25 30
 Ser Glu Pro Thr Thr Val Ala Phe Asp Val Arg Pro Gly Gly Val Val
 35 40 45
 His Ser Phe Ser His Asn Val Gly Pro Gly Asp Lys Tyr Thr Cys Met
 50 55 60
 Phe Thr Tyr Ala Ser Gln Gly Gly Thr Asn Glu Gln Trp Gln Met Ser
 65 70 75 80
 Leu Gly Thr Ser Glu Asp His Gln His Phe Thr Cys Thr Ile Trp Arg

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71
85 90 95
Pro Gln Gly Lys Ser Tyr Leu Tyr Phe Thr Gln Phe Lys Ala Glu Val
100 105 110
Arg Gly Ala Glu Ile Glu Tyr Ala Met Ala Tyr Ser Lys Ala Ala Phe
115 120 125
Glu Arg Glu Ser Asp Val Pro Leu Lys Thr Glu Glu Phe Glu Val Thr
130 135 140
Lys Thr Ala Val Ala His Arg Pro Gly Ala Phe Lys Ala Glu Leu Ser
145 150 155 160
Lys Leu Val Ile Val Ala Lys Ala Ser Arg Thr Glu Leu
165 170

Sequence No.: 6

Sequence length: 73

Sequence type: Amino acid

Topology: Linear

Sequence kind: Protein

Hypothetical: No

Original source:

Organism species: *Homo sapiens*

Cell kind: Epidermoid carcinoma

Cell line: KB

Clone name: HP10189

Sequence description

Met Gly Val Lys Leu Glu Ile Phe Arg Met Ile Ile Tyr Leu Thr Phe
1 5 10 15
Pro Val Ala Met Phe Trp Val Ser Asn Gln Ala Glu Trp Phe Glu Asp
20 25 30
Asp Val Ile Gln Arg Lys Arg Glu Leu Trp Pro Pro Glu Lys Leu Gln

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72

35 40 45
 Glu Ile Glu Glu Phe Lys Glu Arg Leu Arg Lys Arg Arg Glu Glu Lys
 50 55 60
 Leu Leu Arg Asp Ala Gln Gln Asn Ser
 65 70

Sequence No.: 7

Sequence length: 1172

Sequence type: Amino acid

Topology: Linear

Sequence kind: Protein

Hypothetical: No

Original source:

Organism species: *Homo sapiens*

Cell kind: Histiocyte lymphoma

Cell line: U937

Clone name: HP10269

Sequence description

Met Arg Pro Phe Phe Leu Leu Cys Phe Ala Leu Pro Gly Leu Leu His
 1 5 10 15
 Ala Gln Gln Ala Cys Ser Arg Gly Ala Cys Tyr Pro Pro Val Gly Asp
 20 25 30
 Leu Leu Val Gly Arg Thr Arg Phe Leu Arg Ala Ser Ser Thr Cys Gly
 35 40 45
 Leu Thr Lys Pro Glu Thr Tyr Cys Thr Gln Tyr Gly Glu Trp Gln Met
 50 55 60
 Lys Cys Cys Lys Cys Asp Ser Arg Gln Pro His Asn Tyr Tyr Ser His
 65 70 75 80
 Arg Val Glu Asn Val Ala Ser Ser Ser Gly Pro Met Arg Trp Trp Gln

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73

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Ser Gln Asn Asp Val Asn Pro Val Ser Leu Gln Leu Asp Leu Asp Arg

100

105

110

Arg Phe Gln Leu Gln Glu Val Met Met Glu Phe Gln Gly Pro Met Pro

115

120

125

Ala Gly Met Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp Arg

130

135

140

Val Tyr Gln Tyr Leu Ala Ala Asp Cys Thr Ser Thr Phe Pro Arg Val

145

150

155

160

Arg Gln Gly Arg Pro Gln Ser Trp Gln Asp Val Arg Cys Gln Ser Leu

165

170

175

Pro Gln Arg Pro Asn Ala Arg Leu Asn Gly Gly Lys Val Gln Leu Asn

180

185

190

Leu Met Asp Leu Val Ser Gly Ile Pro Ala Thr Gln Ser Gln Lys Ile

195

200

205

Gln Glu Val Gly Glu Ile Thr Asn Leu Arg Val Asn Phe Thr Arg Leu

210

215

220

Ala Pro Val Pro Gln Arg Gly Tyr His Pro Pro Ser Ala Tyr Tyr Ala

225

230

235

240

Val Ser Gln Leu Arg Leu Gln Gly Ser Cys Phe Cys His Gly His Ala

245

250

255

Asp Arg Cys Ala Pro Lys Pro Gly Ala Ser Ala Gly Pro Ser Thr Ala

260

265

270

Val Gln Val His Asp Val Cys Val Cys Gln His Asn Thr Ala Gly Pro

275

280

285

Asn Cys Glu Arg Cys Ala Pro Phe Tyr Asn Asn Arg Pro Trp Arg Pro

290

295

300

Ala Glu Gly Gln Asp Ala His Glu Cys Gln Arg Cys Asp Cys Asn Gly

305

310

315

320

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74

His Ser Glu Thr Cys His Phe Asp Pro Ala Val Phe Ala Ala Ser Gln

325

330

335

Gly Ala Tyr Gly Gly Val Cys Asp Asn Cys Arg Asp His Thr Glu Gly

340

345

350

Lys Asn Cys Glu Arg Cys Gln Leu His Tyr Phe Arg Asn Arg Arg Pro

355

360

365

Gly Ala Ser Ile Gln Glu Thr Cys Ile Ser Cys Glu Cys Asp Pro Asp

370

375

380

Gly Ala Val Pro Gly Ala Pro Cys Asp Pro Val Thr Gly Gln Cys Val

385

390

395

400

Cys Lys Glu His Val Gln Gly Glu Arg Cys Asp Leu Cys Lys Pro Gly

405

410

415

Phe Thr Gly Leu Thr Tyr Ala Asn Pro Gln Gly Cys His Arg Cys Asp

420

425

430

Cys Asn Ile Leu Gly Ser Arg Arg Asp Met Pro Cys Asp Glu Glu Ser

435

440

445

Gly Arg Cys Leu Cys Leu Pro Asn Val Val Gly Pro Lys Cys Asp Gln

450

455

460

Cys Ala Pro Tyr His Trp Lys Leu Ala Ser Gly Gln Gly Cys Glu Pro

465

470

475

480

Cys Ala Cys Asp Pro His Asn Ser Leu Ser Pro Gln Cys Asn Gln Phe

485

490

495

Thr Gly Gln Cys Pro Cys Arg Glu Gly Phe Gly Gly Leu Met Cys Ser

500

505

510

Ala Ala Ala Ile Arg Gln Cys Pro Asp Arg Thr Tyr Gly Asp Val Ala

515

520

525

Thr Gly Cys Arg Ala Cys Asp Cys Asp Phe Arg Gly Thr Glu Gly Pro

530

535

540

Gly Cys Asp Lys Ala Ser Gly Arg Cys Leu Cys Arg Pro Gly Leu Thr

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75

| | | | |
|---|-----|-----|-----|
| 545 | 550 | 555 | 560 |
| Gly Pro Arg Cys Asp Gln Cys Gln Arg Gly Tyr Cys Asn Arg Tyr Pro | | | |
| 565 | 570 | 575 | |
| Val Cys Val Ala Cys His Pro Cys Phe Gln Thr Tyr Asp Ala Asp Leu | | | |
| 580 | 585 | 590 | |
| Arg Glu Gln Ala Leu Arg Phe Gly Arg Leu Arg Asn Ala Thr Ala Ser | | | |
| 595 | 600 | 605 | |
| Leu Trp Ser Gly Pro Gly Leu Glu Asp Arg Gly Leu Ala Ser Arg Ile | | | |
| 610 | 615 | 620 | |
| Leu Asp Ala Lys Ser Lys Ile Glu Gln Ile Arg Ala Val Leu Ser Ser | | | |
| 625 | 630 | 635 | 640 |
| Pro Ala Val Thr Glu Gln Glu Val Ala Gln Val Ala Ser Ala Ile Leu | | | |
| 645 | 650 | 655 | |
| Ser Leu Arg Arg Thr Leu Gln Gly Leu Gln Leu Asp Leu Pro Leu Glu | | | |
| 660 | 665 | 670 | |
| Glu Glu Thr Leu Ser Leu Pro Arg Asp Leu Glu Ser Leu Asp Arg Ser | | | |
| 675 | 680 | 685 | |
| Phe Asn Gly Leu Leu Thr Met Tyr Gln Arg Lys Arg Glu Gln Phe Glu | | | |
| 690 | 695 | 700 | |
| Lys Ile Ser Ser Ala Asp Pro Ser Gly Ala Phe Arg Met Leu Ser Thr | | | |
| 705 | 710 | 715 | 720 |
| Ala Tyr Glu Gln Ser Ala Gln Ala Ala Gln Gln Val Ser Asp Ser Ser | | | |
| 725 | 730 | 735 | |
| Arg Leu Leu Asp Gln Leu Arg Asp Ser Arg Arg Glu Ala Glu Arg Leu | | | |
| 740 | 745 | 750 | |
| Val Arg Gln Ala Gly Gly Gly Gly Gly Thr Gly Ser Pro Lys Leu Val | | | |
| 755 | 760 | 765 | |
| Ala Leu Arg Leu Glu Met Ser Ser Leu Pro Asp Leu Thr Pro Thr Phe | | | |
| 770 | 775 | 780 | |

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76

Asn Lys Leu Cys Gly Asn Ser Arg Gln Met Ala Cys Thr Pro Ile Ser
785 790 795 800
Cys Pro Gly Glu Leu Cys Pro Gln Asp Asn Gly Thr Ala Cys Gly Ser
805 810 815
Arg Cys Arg Gly Val Leu Pro Arg Ala Gly Gly Ala Phe Leu Met Ala
820 825 830
Gly Gln Val Ala Glu Gln Leu Arg Gly Phe Asn Ala Gln Leu Gln Arg
835 840 845
Thr Arg Gln Met Ile Arg Ala Ala Glu Glu Ser Ala Ser Gln Ile Gln
850 855 860
Ser Ser Ala Gln Arg Leu Glu Thr Gln Val Ser Ala Ser Arg Ser Gln
865 870 875 880
Met Glu Glu Asp Val Arg Arg Thr Arg Leu Leu Ile Gln Gln Val Arg
885 890 895
Asp Phe Leu Thr Asp Pro Asp Thr Asp Ala Ala Thr Ile Gln Glu Val
900 905 910
Ser Glu Ala Val Leu Ala Leu Trp Leu Pro Thr Asp Ser Ala Thr Val
915 920 925
Leu Gln Lys Met Asn Glu Ile Gln Ala Ile Ala Ala Arg Leu Pro Asn
930 935 940
Val Asp Leu Val Leu Ser Gln Thr Lys Gln Asp Ile Ala Arg Ala Arg
945 950 955 960
Arg Leu Gln Ala Glu Ala Glu Glu Ala Arg Ser Arg Ala His Ala Val
965 970 975
Glu Gly Gln Val Glu Asp Val Val Gly Asn Leu Arg Gln Gly Thr Val
980 985 990
Ala Leu Gln Glu Ala Gln Asp Thr Met Gln Gly Thr Ser Arg Ser Leu
995 1000 1005
Arg Leu Ile Gln Asp Arg Val Ala Glu Val Gln Gln Val Leu Arg Pro

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77

1010 1015 1020
Ala Glu Lys Leu Val Thr Ser Met Thr Lys Gln Leu Gly Asp Phe Trp
1025 1030 1035 1040
Thr Arg Met Glu Glu Leu Arg His Gln Ala Arg Gln Gln Gly Ala Glu
1045 1050 1055
Ala Val Gln Ala Gln Gln Leu Ala Glu Gly Ala Ser Glu Gln Ala Leu
1060 1065 1070
Ser Ala Gln Glu Gly Phe Glu Arg Ile Lys Gln Lys Tyr Ala Glu Leu
1075 1080 1085
Lys Asp Arg Leu Gly Gln Ser Ser Met Leu Gly Glu Gln Gly Ala Arg
1090 1095 1100
Ile Gln Ser Val Lys Thr Glu Ala Glu Glu Leu Phe Gly Glu Thr Met
1105 1110 1115 1120
Glu Met Met Asp Arg Met Lys Asp Met Glu Leu Glu Leu Leu Arg Gly
1125 1130 1135
Ser Gln Ala Ile Met Leu Arg Ser Ala Asp Leu Thr Gly Leu Glu Lys
1140 1145 1150
Arg Val Glu Gln Ile Arg Asp His Ile Asn Gly Arg Val Leu Tyr Tyr
1155 1160 1165
Ala Thr Cys Lys
1170

Sequence No.: 8

Sequence length: 122

Sequence type: Amino acid

Topology: Linear

Sequence kind: Protein

Hypothetical: No

Original source:

78

Organism species: *Homo sapiens*

Cell kind: Stomach cancer

Clone name: HP10298

Sequence description

Met Gly Leu Leu Leu Leu Val Pro Leu Leu Leu Leu Pro Gly Ser Tyr

1 5 10 15

Gly Leu Pro Phe Tyr Asn Gly Phe Tyr Tyr Ser Asn Ser Ala Asn Asp

20 25 30

Gln Asn Leu Gly Asn Gly His Gly Lys Asp Leu Leu Asn Gly Val Lys

35 40 45

Leu Val Val Glu Thr Pro Glu Glu Thr Leu Phe Thr Arg Ile Leu Thr

50 55 60

Val Gly Pro Gln Ser Leu Gly Ser Glu Ala Leu Ala Ser Pro Thr Arg

65 70 75 80

Arg Ala Ala Cys Thr Val Phe Thr Ala Thr Ala Ser Thr Arg Thr Trp

85 90 95

Gly Pro Pro Leu Pro His Ser Leu Thr Gly Cys Val Phe Ile Glu Trp

100 105 110

Phe Val Phe Pro Cys Gly Leu Glu Pro Phe

115 120

Sequence No.: 9

Sequence length: 175

Sequence type: Amino acid

Topology: Linear

Sequence kind: Protein

Hypothetical: No

Original source:

Organism species: *Homo sapiens*

09354760-041699

Cell kind: Stomach cancer

Clone name: HP10368

Sequence description

Met Glu Lys Ile Pro Val Ser Ala Phe Leu Leu Leu Val Ala Leu Ser
1 5 10 15
Tyr Thr Leu Ala Arg Asp Thr Thr Val Lys Pro Gly Ala Lys Lys Asp
20 25 30
Thr Lys Asp Ser Arg Pro Lys Leu Pro Gln Thr Leu Ser Arg Gly Trp
35 40 45
Gly Asp Gln Leu Ile Trp Thr Gln Thr Tyr Glu Glu Ala Leu Tyr Lys
50 55 60
Ser Lys Thr Ser Asn Lys Pro Leu Met Ile Ile His His Leu Asp Glu
65 70 75 80
Cys Pro His Ser Gln Ala Leu Lys Lys Val Phe Ala Glu Asn Lys Glu
85 90 95
Ile Gln Lys Leu Ala Glu Gln Phe Val Leu Leu Asn Leu Val Tyr Glu
100 105 110
Thr Thr Asp Lys His Leu Ser Pro Asp Gly Gln Tyr Val Pro Arg Ile
115 120 125
Met Phe Val Asp Pro Ser Leu Thr Val Arg Ala Asp Ile Thr Gly Arg
130 135 140
Tyr Ser Asn Arg Leu Tyr Ala Tyr Glu Pro Ala Asp Thr Ala Leu Leu
145 150 155 160
Leu Asp Asn Met Lys Lys Ala Leu Lys Leu Leu Lys Thr Glu Leu
165 170 175

Sequence No.: 10

Sequence length: 462

Sequence type: Nucleic acid

09254760-041699

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Fibrosarcoma

Cell line: HT-1080

Clone name: HP00658

Sequence description

| | |
|---|-----|
| ATGAAGGTCT CCGCGGCAGC CCTCGCTGTC ATCCTCATTG CTACTGCCCT CTGCGCTCCT | 60 |
| GCATCTGCCT CCCCATATTC CTCGGACACC ACACCCTGCT GCTTTGCCTA CATTGCCCCG | 120 |
| CCACTGCCCC GTGCCACAT CAAGGAGTAT TTCTACACCA GTGGCAAGTG CTCCAACCCA | 180 |
| GCAGTCGTCC ACAGGTCAAG GATGCCAAAG AGAGAGGGAC AGCAAGTCTG GCAGGATTTC | 240 |
| CTGTATGACT CCCGGCTGAA CAAGGGCAAG CTTTGTACCC CGAAAGAACC GCCAAGTGTG | 300 |
| TGCCAACCCA GAGAAGAAAT GGGTTCGGGA GTACATCAAC TCTTTGGAGA TGAGCTAGGA | 360 |
| TGGAGAGTCC TTGAACCTGA ACTTACACAA ATTTGCCTGT TTCTGCTTGC TCTTGTCTTA | 420 |
| GCTTGGGAGG CTTCCCCTCA CTATCCTACC CCACCCGCTC CT | 462 |

Sequence No.: 11

Sequence length: 945

Sequence type: Nucleic acid

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Epidermoid carcinoma

Cell line: KB

09254760-044699

Clone name: HP00714

Sequence description

ATGGACCTGC GACAGTTTCT TATGTGCCTG TCCCTGTGCA CAGCCTTTGC CTTGAGCAAA 60
CCCACAGAAA AGAAGGACCG TGTACATCAT GAGCCTCAGC TCAGTGACAA GGTTCACAAT 120
GATGCTCAGA GTTTTGATTA TGACCATGAT GCCTTCTTGG GTGCTGAAGA AGCAAAGACC 180
TTTGATCAGC TGACACCAGA AGAGAGCAAG GAAAGGCTTG GAAAGATTGT AAGTAAAATA 240
GATGGCGACA AGGACGGGTT TGTCACTGTG GATGAGCTCA AAGACTGGAT TAAATTTGCA 300
CAAAAGCGCT GGATTTACGA GGATGTAGAG CGACAGTGGA AGGGGCATGA CCTCAATGAG 360
GACGGCCTCG TTTCCTGGGA GGAGTATAAA AATGCCACCT ACGGCTACGT TTTAGATGAT 420
CCAGATCCTG ATGATGGATT TAACTATAAA CAGATGATGG TTAGAGATGA GCGGAGGTTT 480
AAAATGGCAG ACAAGGATGG AGACCTCATT GCCACCAAGG AGGAGTTCAC AGCTTTCCTG 540
CACCTGAGG AGTATGACTA CATGAAAGAT ATAGTAGTAC AGGAAACAAT GGAAGATATA 600
GATAAGAATG CTGATGGTTT CATTGATCTA GAAGAGTATA TTGGTGACAT GTACAGCCAT 660
GATGGGAATA CTGATGAGCC AGAATGGGTA AAGACAGAGC GAGAGCAGTT TGTTGAGTTT 720
CGGGATAAGA ACCGTGATGG GAAGATGGAC AAGGAAGAGA CCAAAGACTG GATCCTTCCC 780
TCAGACTATG ATCATGCAGA GGCAGAAGCC AGGCACCTGG TCTATGAATC AGACCAAAAC 840
AAGGATGGCA AGCTTACCAA GGAGGAGATC GTTGACAAGT ATGACTTATT TGTTGGCAGC 900
CAGGCCACAG ATTTTGGGGA GGCCTTAGTA CGGCATGATG AGTTC 945

Sequence No.: 12

Sequence length: 474

Sequence type: Nucleic acid

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Stomach cancer

Clone name: HP00876

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Sequence description

ATGGCTTCCA GAAGCATGCG GCTGCTCCTA TTGCTGAGCT GCCTGGCCAA AACAGGAGTC 60
CTGGGTGATA TCATCATGAG ACCCAGCTGT GCTCCTGGAT GGTTTACCA CAAGTCCAAT 120
TGCTATGGTT ACTTCAGGAA GCTGAGGAAC TGGTCTGATG CCGAGCTCGA GTGTCAGTCT 180
TACGGAAACG GAGCCCACCT GGCATCTATC CTGAGTTTAA AGGAAGCCAG CACCATAGCA 240
GAGTACATAA GTGGCTATCA GAGAAGCCAG CCGATATGGA TTGGCCTGCA CGACCCACAG 300
AAGAGGCAGC AGTGGCAGTG GATTGATGGG GCCATGTATC TGTACAGATC CTGGTCTGGC 360
AAGTCCATGG GTGGGAACAA GCACTGTGCT GAGATGAGCT CCAATAACAA CTTTTTAACT 420
TGGAGCAGCA ACGAATGCAA CAAGCGCCAA CACTTCCTGT GCAAGTACCG ACCA 474

Sequence No.: 13

Sequence length: 1128

Sequence type: Nucleic acid

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Liver

Clone name: HP01134

Sequence description

ATGGTTTGGG AAGTAGCTGT ATTCCTCAGT GTGGCCCTGG GCATTGGTGC CGTTCCTATA 60
GATGATCCTG AAGATGGAGG CAAGCACTGG GTGGTGATCG TGGCAGGTTT AAATGGCTGG 120
TATAATTATA GGCACCAGGC AGACGCGTGC CATGCCTACC AGATCATTCA CCGCAATGGG 180
ATTCCTGACG AACAGATCGT TGTGATGATG TACGATGACA TTGCTTACTC TGAAGACAAT 240
CCCACTCCAG GAATTGTGAT CAACAGGCCC AATGGCACAG ATGTCTATCA GGGAGTCCCG 300
AAGGACTACA CTGGAGAGGA TGTTACCCCA CAAAATTTCC TTGCTGTGTT GAGAGGCGAT 360
GCAGAAGCAG TGAAGGGCAT AGGATCCGGC AAAGTCCTGA AGAGTGGCCC CCAGGATCAC 420
GTGTTTCAAT ACTTCACTGA CCATGGATCT ACTGGAATAC TGGTTTTTCC CAATGAAGAT 480

CTTCATGTAA AGGACCTGAA TGAGACCATC CATTACATGT ACAAACACAA AATGTACCGA 540
AAGATGGTGT TCTACATTGA AGCCTGTGAG TCTGGGTCCA TGATGAACCA CCTGCCGGAT 600
AACATCAATG TTTATGCAAC TACTGCTGCC AACCCCAGAG AGTCGTCCTA CGCCTGTTAC 660
TATGATGAGA AGAGGTCCAC GTACCTGGGG GACTGGTACA GCGTCAACTG GATGGAAGAC 720
TCGGACGTGG AAGATCTGAC TAAAGAGACC CTGCACAAGC AGTACCACCT GGTAATAATCG 780
CACACCAACA CCAGCCACGT CATGCAGTAT GGAAACAAAA CAATCTCCAC CATGAAAGTG 840
ATGCAGTTTC AGGGTATGAA ACGCAAAGCC AGTTCTCCCG TCCCCCTACC TCCAGTCACA 900
CACCTTGACC TCACCCCCAG CCCTGATGTG CCTCTCACCA TCATGAAAAG GAAACTGATG 960
AACACCAATG ATCTGGAGGA GTCCAGGCAG CTCACGGAGG AGATCCAGCG GCATCTGGAT 1020
TACGAGTATG CGTTGAGACA TTTGTACGTG CTGGTCAACC TTTGTGAGAA GCCGTATCCG 1080
CTTCACAGGA TAAAATTGTC CATGGACCAC GTGTGCCTTG GTCACTAC 1128

Sequence No.: 14

Sequence length: 519

Sequence type: Nucleic acid

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Epidermoid carcinoma

Cell line: KB

Clone name: HP10029

Sequence description

ATGGCGGCGC CCAGCGGAGG GTGGAACGGC GTCCGCGCGA GCTTGTGGGC CGCGCTGCTC 60
CTAGGGGCCG TGGCGCTGAG GCCGGCGGAG GCGGTGTCCG AGCCCACGAC CGTGGCGTTT 120
GACGTGCGGC CCGGCGGCGT CGTGCAATTCC TTCTCCCAT ACGTGGGCCC GGGGGACAAA 180
TATACGTGTA TGTTCACTTA CGCCTCTCAA GGAGGGACCA ATGAGCAATG GCAGATGAGT 240
CTGGGGACCA GCGAAGACCA CCAGCACTTC ACCTGCACCA TCTGGAGGCC CCAGGGGAAG 300

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TCCTATCTGT ACTTCACACA GTTCAAGGCA GAGGTGCGGG GCGCTGAGAT TGAGTACGCC 360
ATGGCCTACT CTAAAGCCGC ATTTGAAAGG GAAAGTGATG TCCCTCTGAA AACTGAGGAA 420
TTTGAAGTGA CCAAAACAGC AGTGGCTCAC AGGCCCGGGG CATTCAAAGC TGAGCTGTCC 480
AAGCTGGTGA TTGTGGCCAA GGCATCGCGC ACTGAGCTG 519

Sequence No.: 15

Sequence length: 219

Sequence type: Nucleic acid

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Epidermoid carcinoma

Cell line: KB

Clone name: HP10189

Sequence description

ATGGGGGTGA AGCTGGAGAT ATTTCCGATG ATAATCTACC TCACTTTCCC TGTGGCTATG 60
TTCTGGGTTT CCAATCAGGC CGAGTGGTTT GAGGACGATG TCATACAGCG CAAGAGGGAG 120
CTGTGGCCAC CTGAGAAGCT TCAAGAGATA GAGGAATTCA AAGAGAGGTT ACGGAAGCGG 180
CGGGAGGAGA AGCTCCTTCG CGACGCCAG CAGAACTCC 219

Sequence No.: 16

Sequence length: 3516

Sequence type: Nucleic acid

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Lymphoma

Cell line: U937

Clone name: HP10269

Sequence description

ATGAGACCAT TCTTCCTCTT GTGTTTTGCC CTGCCTGGCC TCCTGCATGC CCAACAAGCC 60
TGCTCCCGTG GGGCCTGCTA TCCACCTGTT GGGGACCTGC TTGTTGGGAG GACCCGGTTT 120
CTCCGAGCTT CATCTACCTG TGGACTGACC AAGCCTGAGA CCTACTGCAC CCAGTATGGC 180
GAGTGGCAGA TGAAATGCTG CAAGTGTGAC TCCAGGCAGC CTCACAACTA CTACAGTCAC 240
CGAGTAGAGA ATGTGGCTTC ATCCTCCGGC CCCATGCGCT GGTGGCAGTC CCAGAATGAT 300
GTGAACCCTG TCTCTCTGCA GCTGGACCTG GACAGGAGAT TCCAGCTTCA AGAAGTCATG 360
ATGGAGTTCC AGGGGCCCAT GCCTGCCGGC ATGCTGATTG AGCGCTCCTC AGACTTCGGT 420
AAGACCTGGC GAGTGTACCA GTACCTGGCT GCCGACTGCA CCTCCACCTT CCCTCGGGTC 480
CGCCAGGGTC GGCCTCAGAG CTGGCAGGAT GTTCGGTGCC AGTCCCTGCC TCAGAGGCCT 540
AATGCACGCC TAAATGGGGG GAAGGTCCAA CTTAACCTTA TGGATTTAGT GTCTGGGATT 600
CCAGCAACTC AAAGTCAAAA AATTCAAGAG GTGGGGGAGA TCACAACTT GAGAGTCAAT 660
TTCACCAGGC TGGCCCCTGT GCCCCAAAGG GGCTACCACC CTCCCAGCGC CTACTATGCT 720
GTGTCCCAGC TCCGTCTGCA GGGGAGCTGC TTCTGTCACG GCCATGCTGA TCGCTGCGCA 780
CCCAAGCCTG GGGCCTCTGC AGGCCCTCC ACCGCTGTGC AGGTCCACGA TGTCTGTGTC 840
TGCCAGCACA ACACTGCCGG CCCAAATTGT GAGCGCTGTG CACCCTTCTA CAACAACCGG 900
CCCTGGAGAC CGGCGGAGGG CCAGGACGCC CATGAATGCC AAAGGTGCGA CTGCAATGGG 960
CACTCAGAGA CATGTCACCTT TGACCCCGCT GTGTTTGCCG CCAGCCAGGG GGCATATGGA 1020
GGTGTGTGTG ACAATTGCCG GGACCACACC GAAGGCAAGA ACTGTGAGCG GTGTCAGCTG 1080
CACTATTTCC GGAACCGGCG CCCGGGAGCT TCCATTGAGG AGACCTGCAT CTCCTGCGAG 1140
TGTGATCCGG ATGGGGCAGT GCCAGGGGCT CCCTGTGACC CAGTGACCGG GCAGTGTGTG 1200
TGCAAGGAGC ATGTGCAGGG AGAGCGCTGT GACCTATGCA AGCCGGGCTT CACTGGACTC 1260
ACCTACGCCA ACCCGCAGGG CTGCCACCGC TGTGACTGCA ACATCCTGGG GTCCCGGAGG 1320
GACATGCCGT GTGACGAGGA GAGTGGGCGC TGCCTTTGTC TGCCCAACGT GGTGGGTCCC 1380
AAATGTGACC AGTGTGCTCC CTACCACTGG AAGCTGGCCA GTGGCCAGGG CTGTGAACCG 1440

TGTGCCTGCG ACCCGCACAA CTCCTCAGC CCACAGTGCA ACCAGTTCAC AGGGCAGTGC 1500
CCCTGTCGGG AAGGCTTTGG TGGCCTGATG TGCAGCGCTG CAGCCATCCG CCAGTGTCCA 1560
GACCGGACCT ATGGAGACGT GGCCACAGGA TGCCGAGCCT GTGACTGTGA TTTCCGGGGA 1620
ACAGAGGGCC CGGGCTGCGA CAAGGCATCA GGCCGCTGCC TCTGCCGCCC TGGCTTGACC 1680
GGGCCCCGCT GTGACCAGTG CCAGCGAGGC TACTGCAATC GCTACCCGGT GTGCGTGGCC 1740
TGCCACCCTT GCTTCCAGAC CTATGATGCG GACCTCCGGG AGCAGGCCCT GCGCTTTGGT 1800
AGACTCCGCA ATGCCACCGC CAGCCTGTGG TCAGGGCCTG GGCTGGAGGA CCGTGGCCTG 1860
GCCTCCCGGA TCCTAGATGC AAAGAGTAAG ATTGAGCAGA TCCGAGCAGT TCTCAGCAGC 1920
CCCGCAGTCA CAGAGCAGGA GGTGGCTCAG GTGGCCAGTG CCATCCTCTC CCTCAGGCGA 1980
ACTCTCCAGG GCCTGCAGCT GGATCTGCCC CTGGAGGAGG AGACGTTGTC CCTTCCGAGA 2040
GACCTGGAGA GTCTTGACAG AAGCTTCAAT GGTCTCCTTA CTATGIATCA GAGGAAGAGG 2100
GAGCAGTTTG AAAAAATAAG CAGTGCTGAT CCTTCAGGAG CCTTCCGGAT GCTGAGCACA 2160
GCCTACGAGC AGTCAGCCCA GGCTGCTCAG CAGGTCTCCG ACAGCTCGCG CCTTTTGGAC 2220
CAGCTCAGGG ACAGCCGGAG AGAGGCAGAG AGGCTGGTGC GGCAGGCGGG AGGAGGAGGA 2280
GGCACCGGCA GCCCCAAGCT TGTGGCCCTG AGGCTGGAGA TGTCTTCGTT GCCTGACCTG 2340
ACACCCACCT TCAACAAGCT CTGTGGCAAC TCCAGGCAGA TGGCTTGACAC CCCAATATCA 2400
TGCCCTGGTG AGCTATGTCC CCAAGACAAT GGCACAGCCT GTGGCTCCCG CTGCAGGGGT 2460
GTCCTTCCCA GGGCCGGTGG GGCCTTCTTG ATGGCGGGGC AGGTGGCTGA GCAGCTGCGG 2520
GGCTTCAATG CCCAGCTCCA GCGGACCAGG CAGATGATTA GGGCAGCCGA GGAATCTGCC 2580
TCACAGATTC AATCCAGTGC CCAGCGCTTG GAGACCCAGG TGAGCGCCAG CCGCTCCCAG 2640
ATGGAGGAAG ATGTCAGACG CACACGGCTC CTAATCCAGC AGGTCCGGGA CTTCCTAACA 2700
GACCCCGACA CTGATGCAGC CACTATCCAG GAGGTCAGCG AGGCCGTGCT GGCCCTGTGG 2760
CTGCCCACAG ACTCAGCTAC TGTTCTGCAG AAGATGAATG AGATCCAGGC CATTGCAGCC 2820
AGGCTCCCCA ACGTGGACTT GGTGCTGTCC CAGACCAAGC AGGACATTGC GCGTGCCCGC 2880
CGGTTGCAGG CTGAGGCTGA GGAAGCCAGG AGCCGAGCCC ATGCAGTGGA GGGCCAGGTG 2940
GAAGATGTGG TTGGGAACCT GCGGCAGGGG ACAGTGGCAC TGCAGGAAGC TCAGGACACC 3000
ATGCAAGGCA CCAGCCGCTC CCTTCGGCTT ATCCAGGACA GGGTTGCTGA GGTTTCAGCAG 3060
GTACTGCGGC CAGCAGAAAA GCTGGTGACA AGCATGACCA AGCAGCTGGG TGAATTCTGG 3120
ACACGGATGG AGGAGCTCCG CCACCAAGCC CGGCAGCAGG GGGCAGAGGC AGTCCAGGCC 3180

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CAGCAGCTTG CGGAAGGTGC CAGCGAGCAG GCATTGAGTG CCCAAGAGGG ATTTGAGAGA 3240
ATAAAACAAA AGTATGCTGA GTTGAAGGAC CGGTTGGGTC AGAGTTCCAT GCTGGGTGAG 3300
CAGGGTGCCC GGATCCAGAG TGTGAAGACA GAGGCAGAGG AGCTGTTTGG GGAGACCATG 3360
GAGATGATGG ACAGGATGAA AGACATGGAG TTGGAGCTGC TCGGGGGCAG CCAGGCCATC 3420
ATGCTGCGCT CAGCGGACCT GACAGGACTG GAGAAGCGTG TGGAGCAGAT CCGTGACCAC 3480
ATCAATGGGC GCGTGCTCTA CTATGCCACC TGCAAG 3516

Sequence No.: 17

Sequence length: 366

Sequence type: Nucleic acid

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Stomach cancer

Clone name: HP10298

Sequence description

ATGGGCCTGT TGCTCCTGGT CCCATTGCTC CTGCTGCCCC GCTCCTACGG ACTGCCCTTC 60
TACAACGGCT TCTACTACTC CAACAGCGCC AACGACCAGA ACCTAGGCAA CGGTCATGGC 120
AAAGACCTCC TTAATGGAGT GAAGCTGGTG GTGGAGACAC CCGAGGAGAC CCTGTTACCC 180
CGCATCCTAA CTGTGGGCCC CCAGAGCCTG GGGTCCGAAG CTTTGGCTTC CCCGACCCGC 240
AGAGCCGCTT GTACGGTGTT TACTGCTACC GCCAGCACTA GGACCTGGGG CCCTCCCCTG 300
CCGCATTCCC TCACTGGCTG TGTATTTATT GAGTGGTTCG TTTTCCCTTG TGGGTTGGAG 360
CCATT 366

Sequence No.: 18

Sequence length: 525

Sequence type: Nucleic acid

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Stomach cancer

Clone name: HP10368

Sequence description

ATGGAGAAAA TTCCAGTGTC AGCATTCTTG CTCCTTGTGG CCCTCTCCTA CACTCTGGCC 60
AGAGATACCA CAGTCAAACC TGGAGCCAAA AAGGACACAA AGGACTCTCG ACCCAAAGTG 120
CCCCAGACCC TCTCCAGAGG TTGGGGTGAC CAACTCATCT GGACTCAGAC ATATGAAGAA 180
GCTCTATATA AATCCAAGAC AAGCAACAAA CCCTTGATGA TTATTCATCA CTTGGATGAG 240
TGCCCACACA GTCAAGCTTT AAAGAAAGTG TTTGCTGAAA ATAAAGAAAT CCAGAAATTG 300
GCAGAGCAGT TTGTCCTCCT CAATCTGGTT TATGAAACAA CTGACAAACA CCTTTCTCCT 360
GATGGCCAGT ATGTCCCCAG GATTATGTTT GTTGACCCAT CTCTGACAGT TAGAGCCGAT 420
ATCACTGGAA GATATTCAAA CCGTCTCTAT GCTTACGAAC CTGCAGATAC AGCTCTGTTG 480
CTTGACAACA TGAAGAAAGC TCTCAAGTTG CTGAAGACTG AATTG 525

Sequence No.: 19

Sequence length: 1296

Sequence type: Nucleic acid

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Fibrosarcoma

Cell line: HT-1080

Clone name: HP00658

Sequence characteristics:

Code representing characteristics: CDS

Existence site: 56.. 520

Characterization method: E

Sequence description

| | |
|--|-----|
| CCTGCAGAGG ATCAAGACAG CACGTGGACC TCGCACAGCC TCTCCCACAG GTACC ATG | 58 |
| Met | |
| 1 | |
| AAG GTC TCC GCG GCA GCC CTC GCT GTC ATC CTC ATT GCT ACT GCC CTC | 106 |
| Lys Val Ser Ala Ala Ala Leu Ala Val Ile Leu Ile Ala Thr Ala Leu | |
| 5 10 15 | |
| TGC GCT CCT GCA TCT GCC TCC CCA TAT TCC TCG GAC ACC ACA CCC TGC | 154 |
| Cys Ala Pro Ala Ser Ala Ser Pro Tyr Ser Ser Asp Thr Thr Pro Cys | |
| 20 25 30 | |
| TGC TTT GCC TAC ATT GCC CGC CCA CTG CCC CGT GCC CAC ATC AAG GAG | 202 |
| Cys Phe Ala Tyr Ile Ala Arg Pro Leu Pro Arg Ala His Ile Lys Glu | |
| 35 40 45 | |
| TAT TTC TAC ACC AGT GGC AAG TGC TCC AAC CCA GCA GTC GTC CAC AGG | 250 |
| Tyr Phe Tyr Thr Ser Gly Lys Cys Ser Asn Pro Ala Val Val His Arg | |
| 50 55 60 65 | |
| TCA AGG ATG CCA AAG AGA GAG GGA CAG CAA GTC TGG CAG GAT TTC CTG | 298 |
| Ser Arg Met Pro Lys Arg Glu Gly Gln Gln Val Trp Gln Asp Phe Leu | |
| 70 75 80 | |
| TAT GAC TCC CGG CTG AAC AAG GGC AAG CTT TGT CAC CCG AAA GAA CCG | 346 |
| Tyr Asp Ser Arg Leu Asn Lys Gly Lys Leu Cys His Pro Lys Glu Pro | |
| 85 90 95 | |
| CCA AGT GTG TGC CAA CCC AGA GAA GAA ATG GGT TCG GGA GTA CAT CAA | 394 |
| Pro Ser Val Cys Gln Pro Arg Glu Glu Met Gly Ser Gly Val His Gln | |
| 100 105 110 | |

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CTC TTT GGA GAT GAG CTA GGA TGG AGA GTC CTT GAA CCT GAA CTT ACA 442
Leu Phe Gly Asp Glu Leu Gly Trp Arg Val Leu Glu Pro Glu Leu Thr
115 120 125
CAA ATT TGC CTG TTT CTG CTT GCT CTT GTC CTA GCT TGG GAG GCT TCC 490
Gln Ile Cys Leu Phe Leu Leu Ala Leu Val Leu Ala Trp Glu Ala Ser
130 135 140 145
CCT CAC TAT CCT ACC CCA CCC GCT CCT TGAAGGGCCC AGA 530
Pro His Tyr Pro Thr Pro Pro Ala Pro
150
TTCTACCACA CAGCAGCAGT TACAAAAACC TTCCCCAGGC TGGACGTGGT GGCTCACGCC 590
TGTAATCCCA GCACTTTGGG AGGCCAAGGT GGGTGGATCA CTTGAGGTCA GGAGTTCGAG 650
ACCAGCCTGG CCAACATGAT GAAACCCCAT CTCTACTAAA AATACAAAAA ATTAGCCGGG 710
CGTGGTAGCG GCGCCTGTA GTCCCAGCTA CTCGGGAGGC TGAGGCAGGA GAATGGCGTG 770
AACCCGGGAG GCGGAGCTTG CAGTGAGCCG AGATCGCGCC ACTGCACTCC AGCCTGGGCG 830
ACAGAGCGAG ACTCCGTCTC AAAAAAAAAA AAAAAAAAAA AAATACAAAA ATTAGCCGGG 890
CGTGGTGGCC CACGCCTGTA ATCCCAGCTA CTCGGGAGGC TAAGGCAGGA AAATTGTTTG 950
AACCCAGGAG GTGGAGGCTG CAGTGAGCTG AGATTGTGCC ACTTCACTCC AGCCTGGGTG 1010
ACAAAGTGAG ACTCCGTCAC AACAACAACA AAAAAAGCT TCCCCAACTA AAGCCTAGAA 1070
GAGCTTCTGA GCGCTGCTT TGTCAAAGG AAGTCTCTAG GTTCTGAGCT CTGGCTTTGC 1130
CTTGGCTTTG CCAGGGCTCT GTGACCAGGA AGGAAGTCAG CATGCCTCTA GAGGCAAGGA 1190
GGGAGGAAC GCTGCACTCT TAAGCTTCCG CCGTCTCAAC CCCTCACAGG AGCTTACTGG 1250
CAAACATGAA AAATCGGCTT ACCATTAAAG TTCTCAATGC AACCAT 1296

Sequence No.: 20

Sequence length: 3311

Sequence type: Nucleic acid

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

095450-041599

Original source:

Organism species: *Homo sapiens*

Cell kind: Epidermoid carcinoma

Cell line: KB

Clone name: HP00714

Sequence characteristics:

Code representing characteristics: CDS

Existence site: 57.. 1004

Characterization method: E

Sequence description

GAGCGGCGGC CACGGCATCC TGTGCTGTGG GGGCTACGAG GAAAGATCTA ATTATC ATG 59
 Met
 1
 GAC CTG CGA CAG TTT CTT ATG TGC CTG TCC CTG TGC ACA GCC TTT GCC 107
 Asp Leu Arg Gln Phe Leu Met Cys Leu Ser Leu Cys Thr Ala Phe Ala
 5 10 15
 TTG AGC AAA CCC ACA GAA AAG AAG GAC CGT GTA CAT CAT GAG CCT CAG 155
 Leu Ser Lys Pro Thr Glu Lys Lys Asp Arg Val His His Glu Pro Gln
 20 25 30
 CTC AGT GAC AAG GTT CAC AAT GAT GCT CAG AGT TTT GAT TAT GAC CAT 203
 Leu Ser Asp Lys Val His Asn Asp Ala Gln Ser Phe Asp Tyr Asp His
 35 40 45
 GAT GCC TTC TTG GGT GCT GAA GAA GCA AAG ACC TTT GAT CAG CTG ACA 251
 Asp Ala Phe Leu Gly Ala Glu Glu Ala Lys Thr Phe Asp Gln Leu Thr
 50 55 60 65
 CCA GAA GAG AGC AAG GAA AGG CTT GGA AAG ATT GTA AGT AAA ATA GAT 299
 Pro Glu Glu Ser Lys Glu Arg Leu Gly Lys Ile Val Ser Lys Ile Asp
 70 75 80
 GGC GAC AAG GAC GGG TTT GTC ACT GTG GAT GAG CTC AAA GAC TGG ATT 347

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Gly Asp Lys Asp Gly Phe Val Thr Val Asp Glu Leu Lys Asp Trp Ile
 85 90 95
 AAA TTT GCA CAA AAG CGC TGG ATT TAC GAG GAT GTA GAG CGA CAG TGG 395
 Lys Phe Ala Gln Lys Arg Trp Ile Tyr Glu Asp Val Glu Arg Gln Trp
 100 105 110
 AAG GGG CAT GAC CTC AAT GAG GAC GGC CTC GTT TCC TGG GAG GAG TAT 443
 Lys Gly His Asp Leu Asn Glu Asp Gly Leu Val Ser Trp Glu Glu Tyr
 115 120 125
 AAA AAT GCC ACC TAC GGC TAC GTT TTA GAT GAT CCA GAT CCT GAT GAT 491
 Lys Asn Ala Thr Tyr Gly Tyr Val Leu Asp Asp Pro Asp Pro Asp Asp
 130 135 140 145
 GGA TTT AAC TAT AAA CAG ATG ATG GTT AGA GAT GAG CGG AGG TTT AAA 539
 Gly Phe Asn Tyr Lys Gln Met Met Val Arg Asp Glu Arg Arg Phe Lys
 150 155 160
 ATG GCA GAC AAG GAT GGA GAC CTC ATT GCC ACC AAG GAG GAG TTC ACA 587
 Met Ala Asp Lys Asp Gly Asp Leu Ile Ala Thr Lys Glu Glu Phe Thr
 165 170 175
 GCT TTC CTG CAC CCT GAG GAG TAT GAC TAC ATG AAA GAT ATA GTA GTA 635
 Ala Phe Leu His Pro Glu Glu Tyr Asp Tyr Met Lys Asp Ile Val Val
 180 185 190
 CAG GAA ACA ATG GAA GAT ATA GAT AAG AAT GCT GAT GGT TTC ATT GAT 683
 Gln Glu Thr Met Glu Asp Ile Asp Lys Asn Ala Asp Gly Phe Ile Asp
 195 200 205
 CTA GAA GAG TAT ATT GGT GAC ATG TAC AGC CAT GAT GGG AAT ACT GAT 731
 Leu Glu Glu Tyr Ile Gly Asp Met Tyr Ser His Asp Gly Asn Thr Asp
 210 215 220 225
 GAG CCA GAA TGG GTA AAG ACA GAG CGA GAG CAG TTT GTT GAG TTT CGG 779
 Glu Pro Glu Trp Val Lys Thr Glu Arg Glu Gln Phe Val Glu Phe Arg
 230 235 240

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GAT AAG AAC CGT GAT GGG AAG ATG GAC AAG GAA GAG ACC AAA GAC TGG 827
Asp Lys Asn Arg Asp Gly Lys Met Asp Lys Glu Glu Thr Lys Asp Trp
245 250 255
ATC CTT CCC TCA GAC TAT GAT CAT GCA GAG GCA GAA GCC AGG CAC CTG 875
Ile Leu Pro Ser Asp Tyr Asp His Ala Glu Ala Glu Ala Arg His Leu
260 265 270
GTC TAT GAA TCA GAC CAA AAC AAG GAT GGC AAG CTT ACC AAG GAG GAG 923
Val Tyr Glu Ser Asp Gln Asn Lys Asp Gly Lys Leu Thr Lys Glu Glu
275 280 285
ATC GTT GAC AAG TAT GAC TTA TTT GTT GGC AGC CAG GCC ACA GAT TTT 971
Ile Val Asp Lys Tyr Asp Leu Phe Val Gly Ser Gln Ala Thr Asp Phe
290 295 300 305
GGG GAG GCC TTA GTA CGG CAT GAT GAG TTC TGAGCTACGG AGGAACCCT 1020
Gly Glu Ala Leu Val Arg His Asp Glu Phe
310 315
CATTTCCTCA AAAGTAATTT ATTTTACAG CTTCTGGTTT CACATGAAAT TGTTTGCGCT 1080
ACTGAGACTG TTACTACAAA CTTTTAAGA CATGAAAAGG CGTAATGAAA ACCATCCCGT 1140
CCCCATTCCT CCTCCTCTCT GAGGGACTGG AGGGAAGCCG TGCTTCTGAG GAACAACTCT 1200
AATTAGTACA CTTGTGTTTG TAGATTTACA CTTTGTATTA TGTATTAACA TGGCGTGTTT 1260
ATTTTGTAT TTTTCTCTGG TTGGGAGTAT GATATGAAGG ATCAAGATCC TCAACTCACA 1320
CATGTAGACA AACATTAGCT CTTTACTCTT TCTCAACCCC TTTTATGATT TTAATAATTC 1380
TCACTTAACT AATTTTGTA GCGTGAGATC AATAAGAAAT GTTCAGGAGA GAGGAAAGAA 1440
AAAAAATATA TGCTCCACAA TTTATATTTA GAGAGAGAAC ACTTAGTCTT GCCTGTCAAA 1500
AAGTCCAACA TTTCATAGGT AGTAGGGGCC ACATATTACA TTCAGTTGCT ATAGGTCCAG 1560
CAACTGAACC TGCCATTACC TGGGCAAGGA AAGATCCCTT TGCTCTAGGA AAGCTTGGCC 1620
CAAATTGATT TTCTTCTTTT TCCCCCTGTA GGAAGTACTG TTGGCTAATT TTGTCAAGCA 1680
CAGCTGTGGT GGGAAGAGTT AGGGCCAGTG TCTTGAAAAT CAATCAAGTA GTGAATGTGA 1740
TCTCTTTGCA GAGCTATAGA TAGAAACAGC TGGAAAATA AAGGAAAAAT ACAAGTGTTT 1800
TCGGGGCATA CATTTTTTTT CTGGGTGTGC ATCTGTTGAA ATGCTCAAGA CTTAATTATT 1860

TGCCTTTTGA AATCACTGTA AATGCCCCCA TCCGGTTCCT CTTCTTCCCA GGTGTGCCAA 1920
GGAATTAATC TTGGTTTCAC TACAATTAAA ATTCACCTCT TTCCAATCAT GTCATTGAAA 1980
GTGCCTTTAA CGAAAGAAAT GGTCAC TGAAATCT CTTAAGAAAC CCTGAGATTA 2040
AAAAAAGACT ATTTGGATAA CTTATAGGAA AGCCTAGAAC CTCCCAGTAG AGTGGGGATT 2100
TTTTTCTTCT TCCCTTTCTC TTTTGGACAA TAGTTAAATT AGCAGTATTA GTTATGAGTT 2160
TGGTTGCAGT GTTCTTATCT TGTGGGCTGA TTTCCAAAAA CCACATGCTG CTGAATTTAC 2220
CAGGGATCCT CATACCTCAC AATGCAAACC ACTTACTACC AGGCCTTTTT CTGTGTCCAC 2280
TGGAGAGCTT GAGCTCACAC TCAAAGATCA GAGGACCTAC AGAGAGGGCT CTTTGGTTTG 2340
AGGACCATGG CTTACCTTTC CTGCCTTTGA CCCATCACAC CCCATTTCTT CCTCTTTCCC 2400
TCTCCCCGCT GCCAAAAAAA AAAAAAAG GAAACGTTA TCATGAATCA ACAGGGTTTC 2460
AGTCCTTATC AAAGAGAGAT GTGGAAAGAG CTAAAGAAAC CACCCTTTGT TCCCAACTCC 2520
ACTTTACCCA TATTTTATGC AACACAAACA CTGTCCTTTT GGGTCCCTTT CTTACAGATG 2580
GACCTCTTGA GAAGAATTAT CGTATTCCAC GTTTTATAGC CTCAGGTAC CAAGATAAAT 2640
ATATGTATAT ATAACCTTAA TTATTGCTAT ATCTTTGTGG ATAATACATT CAGGTGGTGC 2700
TGGGTGATTT ATTATAATCT GAACCTAGGT ATATCCTTTG GTCTTCCACA GTCATGTTGA 2760
GGTGGGCTCC CTGGTATGGT AAAAAGCCAG GTATAATGTA ACTTCACCCC AGCCTTTGTA 2820
CTAAGCTCTT GATAGTGGAT ATACTCTTTT AAGTTTAGCC CCAATATAGG GTAATGGAAA 2880
TTTCTGCCC TCTGGGTTCC CCATTTTAC TATTAAGAAG ACCAGTGATA ATTTAATAAT 2940
GCCACCAACT CTGGCTTAGT TAAGTGAGAG TGTGAAGTGT GTGGCAAGAG AGCCTCACAC 3000
CTCACTAGGT GCAGAGAGCC CAGGCCTTAT GTTAAAATCA TGCACCTGAA AAGCAAACCT 3060
TAATCTGCAA AGACAGCAGC AAGCATTATA CGGTCATCTT GAATGATCCC TTTGAAATTT 3120
TTTTTTTGTT TGTTTGTTTA AATCAAGCCT GAGGCTGGTG AACAGTAGCT ACACACCCAT 3180
ATTGTGTGTT CTGTGAATGC TAGCTTTCTT GAATTTGGAT ATTGGTTATT TTTTATAGAG 3240
TGTAACCAA GTTTTATATT CTGCAATGCG AACAGGTACC TATCTGTTTC TAAATAAAAC 3300
TGTTTACATT C 3311

Sequence No.: 21

Sequence length: 1152

Sequence type: Nucleic acid

0934750.041699

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Stomach cancer

Clone name: HP00876

Sequence characteristics:

Code representing characteristics: CDS

Existence site: 147.. 623

Characterization method: E

Sequence description

| | |
|---|-----|
| ACTGGAGACA CTGAAGAAGG CAGGGGCCCT TAGAGTCTTG GTTGCCAAAC AGATTTCAG | 60 |
| ATCAAGGAGA ACCCAGGAGT TTCAAAGAAG CGCTAGTAAG GTCTCTGAGA TCCTTGCACT | 120 |
| AGCTACATCC TCAGGGTAGG AGGAAG ATG GCT TCC AGA AGC ATG CGG CTG CTC | 173 |
| Met Ala Ser Arg Ser Met Arg Leu Leu | |
| 1 5 | |
| CTA TTG CTG AGC TGC CTG GCC AAA ACA GGA GTC CTG GGT GAT ATC ATC | 221 |
| Leu Leu Leu Ser Cys Leu Ala Lys Thr Gly Val Leu Gly Asp Ile Ile | |
| 10 15 20 25 | |
| ATG AGA CCC AGC TGT GCT CCT GGA TGG TTT TAC CAC AAG TCC AAT TGC | 269 |
| Met Arg Pro Ser Cys Ala Pro Gly Trp Phe Tyr His Lys Ser Asn Cys | |
| 30 35 40 | |
| TAT GGT TAC TTC AGG AAG CTG AGG AAC TGG TCT GAT GCC GAG CTC GAG | 317 |
| Tyr Gly Tyr Phe Arg Lys Leu Arg Asn Trp Ser Asp Ala Glu Leu Glu | |
| 45 50 55 | |
| TGT CAG TCT TAC GGA AAC GGA GCC CAC CTG GCA TCT ATC CTG AGT TTA | 365 |
| Cys Gln Ser Tyr Gly Asn Gly Ala His Leu Ala Ser Ile Leu Ser Leu | |
| 60 65 70 | |

96

AAG GAA GCC AGC ACC ATA GCA GAG TAC ATA AGT GGC TAT CAG AGA AGC 413
 Lys Glu Ala Ser Thr Ile Ala Glu Tyr Ile Ser Gly Tyr Gln Arg Ser
 75 80 85
 CAG CCG ATA TGG ATT GGC CTG CAC GAC CCA CAG AAG AGG CAG CAG TGG 461
 Gln Pro Ile Trp Ile Gly Leu His Asp Pro Gln Lys Arg Gln Gln Trp
 90 95 100 105
 CAG TGG ATT GAT GGG GCC ATG TAT CTG TAC AGA TCC TGG TCT GGC AAG 509
 Gln Trp Ile Asp Gly Ala Met Tyr Leu Tyr Arg Ser Trp Ser Gly Lys
 110 115 120
 TCC ATG GGT GGG AAC AAG CAC TGT GCT GAG ATG AGC TCC AAT AAC AAC 557
 Ser Met Gly Gly Asn Lys His Cys Ala Glu Met Ser Ser Asn Asn Asn
 125 130 135
 TTT TTA ACT TGG AGC AGC AAC GAA TGC AAC AAG CGC CAA CAC TTC CTG 605
 Phe Leu Thr Trp Ser Ser Asn Glu Cys Asn Lys Arg Gln His Phe Leu
 140 145 150
 TGC AAG TAC CGA CCA TAGAGCAAGA ATCAAGATTC TGCTAACTCC 650
 Cys Lys Tyr Arg Pro
 155
 TGCACAGCCC CGTCCTCTTC CTTTCTGCTA GCCTGGCTAA ATCTGCTCAT TATTTTCAGAG 710
 GGGAAACCTA GCAAACCTAAG AGTGATAAGG GCCCTACTAC ACTGGCTTTT TTAGGCTTAG 770
 AGACAGAAAC TTTAGCATTG GCCCAGTAGT GGCTTCTAGC TCTAAATGTT TGCCCCGCCA 830
 TCCCTTTCCA CAGTATCCTT CTTCCCTCCT CCCCTGTCTC TGGCTGTCTC GAGCAGTCTA 890
 GAAGAGTGCA TCTCCAGCCT ATGAAACAGC TGGGTCTTTG GCCATAAGAA GTAAAGATTT 950
 GAAGACAGAA GGAAGAAACT CAGGAGTAAG CTTCTAGCCC CCTTCAGCTT CTACACCCTT 1010
 CTGCCCTCTC TCCATTGCCT GCACCCCACC CCAGCCACTC AACTCCTGCT TGTTTTTCCT 1070
 TTGGCCATGG GAAGGTTTAC CAGTAGAATC CTTGCTAGGT TGATGTGGGC CATAATTCC 1130
 TTTAATAAAC CATTGTGTAC AT 1152

Sequence No.: 22

D 9254750 - 041690

97

Sequence length: 1749

Sequence type: Nucleic acid

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Liver

Clone name: HP01134

Sequence characteristics:

Code representing characteristics: CDS

Existence site: 117.. 1247

Characterization method: E

Sequence description

AATCACAGCA GTNCCGACGT CGTGGGTGTT TGGTGTGAGG CTGCGAGCCG CCGCCGCCAC 60

CACTGCCACC ACGGTCGCCT GCCACAGGTG TCTGCAATTG AACTCCAAGG TGCAGA ATG 119

Met

1

GTT TGG AAA GTA GCT GTA TTC CTC AGT GTG GCC CTG GGC ATT GGT GCC 167

Val Trp Lys Val Ala Val Phe Leu Ser Val Ala Leu Gly Ile Gly Ala

5

10

15

GTT CCT ATA GAT GAT CCT GAA GAT GGA GGC AAG CAC TGG GTG GTG ATC 215

Val Pro Ile Asp Asp Pro Glu Asp Gly Gly Lys His Trp Val Val Ile

20

25

30

GTG GCA GGT TCA AAT GGC TGG TAT AAT TAT AGG CAC CAG GCA GAC GCG 263

Val Ala Gly Ser Asn Gly Trp Tyr Asn Tyr Arg His Gln Ala Asp Ala

35

40

45

TGC CAT GCC TAC CAG ATC ATT CAC CGC AAT GGG ATT CCT GAC GAA CAG 311

Cys His Ala Tyr Gln Ile Ile His Arg Asn Gly Ile Pro Asp Glu Gln

D52543-04169

98

| | | | | |
|---|-----|-----|-----|-----|
| 50 | 55 | 60 | 65 | |
| ATC GTT GTG ATG ATG TAC GAT GAC ATT GCT TAC TCT GAA GAC AAT CCC | | | | 359 |
| Ile Val Val Met Met Tyr Asp Asp Ile Ala Tyr Ser Glu Asp Asn Pro | | | | |
| | 70 | 75 | 80 | |
| ACT CCA GGA ATT GTG ATC AAC AGG CCC AAT GGC ACA GAT GTC TAT CAG | | | | 407 |
| Thr Pro Gly Ile Val Ile Asn Arg Pro Asn Gly Thr Asp Val Tyr Gln | | | | |
| | 85 | 90 | 95 | |
| GGA GTC CCG AAG GAC TAC ACT GGA GAG GAT GTT ACC CCA CAA AAT TTC | | | | 455 |
| Gly Val Pro Lys Asp Tyr Thr Gly Glu Asp Val Thr Pro Gln Asn Phe | | | | |
| | 100 | 105 | 110 | |
| CTT GCT GTG TTG AGA GGC GAT GCA GAA GCA GTG AAG GGC ATA GGA TCC | | | | 503 |
| Leu Ala Val Leu Arg Gly Asp Ala Glu Ala Val Lys Gly Ile Gly Ser | | | | |
| | 115 | 120 | 125 | |
| GGC AAA GTC CTG AAG AGT GGC CCC CAG GAT CAC GTG TTC ATT TAC TTC | | | | 551 |
| Gly Lys Val Leu Lys Ser Gly Pro Gln Asp His Val Phe Ile Tyr Phe | | | | |
| | 130 | 135 | 140 | 145 |
| ACT GAC CAT GGA TCT ACT GGA ATA CTG GTT TTT CCC AAT GAA GAT CTT | | | | 599 |
| Thr Asp His Gly Ser Thr Gly Ile Leu Val Phe Pro Asn Glu Asp Leu | | | | |
| | 150 | 155 | 160 | |
| CAT GTA AAG GAC CTG AAT GAG ACC ATC CAT TAC ATG TAC AAA CAC AAA | | | | 647 |
| His Val Lys Asp Leu Asn Glu Thr Ile His Tyr Met Tyr Lys His Lys | | | | |
| | 165 | 170 | 175 | |
| ATG TAC CGA AAG ATG GTG TTC TAC ATT GAA GCC TGT GAG TCT GGG TCC | | | | 695 |
| Met Tyr Arg Lys Met Val Phe Tyr Ile Glu Ala Cys Glu Ser Gly Ser | | | | |
| | 180 | 185 | 190 | |
| ATG ATG AAC CAC CTG CCG GAT AAC ATC AAT GTT TAT GCA ACT ACT GCT | | | | 743 |
| Met Met Asn His Leu Pro Asp Asn Ile Asn Val Tyr Ala Thr Thr Ala | | | | |
| | 195 | 200 | 205 | |
| GCC AAC CCC AGA GAG TCG TCC TAC GCC TGT TAC TAT GAT GAG AAG AGG | | | | 791 |

095450-04169

Ala Asn Pro Arg Glu Ser Ser Tyr Ala Cys Tyr Tyr Asp Glu Lys Arg
 210 215 220 225
 TCC ACG TAC CTG GGG GAC TGG TAC AGC GTC AAC TGG ATG GAA GAC TCG 839
 Ser Thr Tyr Leu Gly Asp Trp Tyr Ser Val Asn Trp Met Glu Asp Ser
 230 235 240
 GAC GTG GAA GAT CTG ACT AAA GAG ACC CTG CAC AAG CAG TAC CAC CTG 887
 Asp Val Glu Asp Leu Thr Lys Glu Thr Leu His Lys Gln Tyr His Leu
 245 250 255
 GTA AAA TCG CAC ACC AAC ACC AGC CAC GTC ATG CAG TAT GGA AAC AAA 935
 Val Lys Ser His Thr Asn Thr Ser His Val Met Gln Tyr Gly Asn Lys
 260 265 270
 ACA ATC TCC ACC ATG AAA GTG ATG CAG TTT CAG GGT ATG AAA CGC AAA 983
 Thr Ile Ser Thr Met Lys Val Met Gln Phe Gln Gly Met Lys Arg Lys
 275 280 285
 GCC AGT TCT CCC GTC CCC CTA CCT CCA GTC ACA CAC CTT GAC CTC ACC 1031
 Ala Ser Ser Pro Val Pro Leu Pro Pro Val Thr His Leu Asp Leu Thr
 290 295 300 305
 CCC AGC CCT GAT GTG CCT CTC ACC ATC ATG AAA AGG AAA CTG ATG AAC 1079
 Pro Ser Pro Asp Val Pro Leu Thr Ile Met Lys Arg Lys Leu Met Asn
 310 315 320
 ACC AAT GAT CTG GAG GAG TCC AGG CAG CTC ACG GAG GAG ATC CAG CGG 1127
 Thr Asn Asp Leu Glu Glu Ser Arg Gln Leu Thr Glu Glu Ile Gln Arg
 325 330 335
 CAT CTG GAT TAC GAG TAT GCG TTG AGA CAT TTG TAC GTG CTG GTC AAC 1175
 His Leu Asp Tyr Glu Tyr Ala Leu Arg His Leu Tyr Val Leu Val Asn
 340 345 350
 CTT TGT GAG AAG CCG TAT CCG CTT CAC AGG ATA AAA TTG TCC ATG GAC 1223
 Leu Cys Glu Lys Pro Tyr Pro Leu His Arg Ile Lys Leu Ser Met Asp
 355 360 365

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100

CAC GTG TGC CTT GGT CAC TAC TGAAGAGCTG CCTCCTGGAA GCTTTT 1270

His Val Cys Leu Gly His Tyr

370

375

CCAAGTGTGA GCGCCCCACC GACTGTGTGC TGATCAGAGA CTGGAGAGGT GGAGTGAGAA 1330

GTCTCCGCTG CTCGGGCCCT CCTGGGGAGC CCCCGCTCCA GGGCTCGCTC CAGGACCTTC 1390

TTCACAAGAT GACTTGCTCG CTGTTACCTG CTTCCCCAGT CTTTCTGAA AACTACAAA 1450

TTAGGGTGGG AAAAGCTCTG TATTGAGAAG GGTCATATTT GCTTCTAGG AGGTTTGTTG 1510

TTTTGCCTGT TAGTTTTGAG GAGCAGGAAG CTCATGGGGG CTTCTGTAGC CCCTCTCAAA 1570

AGGAGTCTTT ATTCTGAGAA TTTGAAGCTG AAACCTCTTT AAATCTTCAG AATGATTTTA 1630

TTGAAGAGGG CCGCAAGCCC CAAATGGAAA ACTGTTTTTA GAAAATATGA TGATTTTGA 1690

TTGCTTTTGT ATTTAATTCT GCAGGTGTTT AAGTCTTAAA AAATAAAGAT TTATAACAG 1749

Sequence No.: 23

Sequence length: 988

Sequence type: Nucleic acid

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Epidermoid carcinoma

Cell line: KB

Clone name: HP10029

Sequence characteristics:

Code representing characteristics: CDS

Existence site: 9.. 530

Characterization method: E

Sequence description

AGTCCAAC ATG GCG GCG CCC AGC GGA GGG TGG AAC GGC GTC CGC GCG AGC 50

0925450-04159

101

Met Ala Ala Pro Ser Gly Gly Trp Asn Gly Val Arg Ala Ser

| | | | |
|---|-----|-----|-----|
| 1 | 5 | 10 | |
| TTG TGG GCC GCG CTG CTC CTA GGG GCC GTG GCG CTG AGG CCG GCG GAG | 98 | | |
| Leu Trp Ala Ala Leu Leu Leu Gly Ala Val Ala Leu Arg Pro Ala Glu | | | |
| 15 | 20 | 25 | 30 |
| GCG GTG TCC GAG CCC ACG ACC GTG GCG TTT GAC GTG CCG CCC GGC GGC | 146 | | |
| Ala Val Ser Glu Pro Thr Thr Val Ala Phe Asp Val Arg Pro Gly Gly | | | |
| 35 | 40 | 45 | |
| GTC GTG CAT TCC TTC TCC CAT AAC GTG GGC CCG GGG GAC AAA TAT ACG | 194 | | |
| Val Val His Ser Phe Ser His Asn Val Gly Pro Gly Asp Lys Tyr Thr | | | |
| 50 | 55 | 60 | |
| TGT ATG TTC ACT TAC GCC TCT CAA GGA GGG ACC AAT GAG CAA TGG CAG | 242 | | |
| Cys Met Phe Thr Tyr Ala Ser Gln Gly Gly Thr Asn Glu Gln Trp Gln | | | |
| 65 | 70 | 75 | |
| ATG AGT CTG GGG ACC AGC GAA GAC CAC CAG CAC TTC ACC TGC ACC ATC | 290 | | |
| Met Ser Leu Gly Thr Ser Glu Asp His Gln His Phe Thr Cys Thr Ile | | | |
| 80 | 85 | 90 | |
| TGG AGG CCC CAG GGG AAG TCC TAT CTG TAC TTC ACA CAG TTC AAG GCA | 338 | | |
| Trp Arg Pro Gln Gly Lys Ser Tyr Leu Tyr Phe Thr Gln Phe Lys Ala | | | |
| 95 | 100 | 105 | 110 |
| GAG GTG CCG GGC GCT GAG ATT GAG TAC GCC ATG GCC TAC TCT AAA GCC | 386 | | |
| Glu Val Arg Gly Ala Glu Ile Glu Tyr Ala Met Ala Tyr Ser Lys Ala | | | |
| 115 | 120 | 125 | |
| GCA TTT GAA AGG GAA AGT GAT GTC CCT CTG AAA ACT GAG GAA TTT GAA | 434 | | |
| Ala Phe Glu Arg Glu Ser Asp Val Pro Leu Lys Thr Glu Glu Phe Glu | | | |
| 130 | 135 | 140 | |
| GTG ACC AAA ACA GCA GTG GCT CAC AGG CCC GGG GCA TTC AAA GCT GAG | 482 | | |
| Val Thr Lys Thr Ala Val Ala His Arg Pro Gly Ala Phe Lys Ala Glu | | | |
| 145 | 150 | 155 | |

102

CTG TCC AAG CTG GTG ATT GTG GCC AAG GCA TCG CGC ACT GAG CTG 527
Leu Ser Lys Leu Val Ile Val Ala Lys Ala Ser Arg Thr Glu Leu
160 165 170
TGA CCAGCAGCCC TGTTCGCGGT GGCACCTTCT CATCTCCGGT GAAGCTGAAG 580
GGGCCTGTGG CCCTGAAAGG GCCAGCACAT CACTGGTTTT CTAGGAGGGA CTCTTAAGTT 640
TTCTACCTGG GCTGACGTTG CCTTGTCCGG AGGGGCTTGC AGGGTGGCTG AAGCCCTGGG 700
GCAGAGAACA GAGGGTCCAG GGCCCTCCTG GCTCCCAACA GCTTCTCAGT TCCCACTTCC 760
TGCTGAGCTC TTCTGGACTC AGGATCGCAG ATCCGGGGCA CAAAGAGGGT GGGGAACATG 820
GGGGCTATGC TGGGGAAAGC AGCCATGCTC CCCCCGACCT CCAGCCGAGC ATCCTTCATG 880
AGCCTGCAGA ACTGCTTTCC TATGTTTACC CAGGGGACCT CCTTTCAGAT GAACTGGGAA 940
GAGATGAAAT GTTTTTTCAT ATTTAAATAA ATAAGAACAT TAAAAAGC 988

Sequence No.: 24

Sequence length: 390

Sequence type: Nucleic acid

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Epidermoid carcinoma

Cell line: KB

Clone name: HP10189

Sequence characteristics:

Code representing characteristics: CDS

Existence site: 102.. 323

Characterization method: E

Sequence description

AATCAGCTTC AGCAATGGAG CGTGCAAAAC ACCAGTGAGC TTCTGTCTTG CTGGAGGGTC 60

D5E54350-041699

103

| | | | | | | | | | | |
|---------------------|------------|------------|------------|------------|------------|-------------|-----|-----|-----|-----|
| GGCTTTGGGC GGA | ACTGGCT | TTGTTGACCG | GGAGAAACGA | G | ATG | GGG | GTG | AAG | CTG | 116 |
| Met Gly Val Lys Leu | | | | | | | | | | |
| 1 5 | | | | | | | | | | |
| GAG | ATA | TTT | CGG | ATG | ATA | ATC | TAC | CTC | ACT | 164 |
| Glu | Ile | Phe | Arg | Met | Ile | Ile | Tyr | Leu | Thr | |
| 10 15 20 | | | | | | | | | | |
| TGG | GTT | TCC | AAT | CAG | GCC | GAG | TGG | TTT | GAG | 212 |
| Trp | Val | Ser | Asn | Gln | Ala | Glu | Trp | Phe | Glu | |
| 25 30 35 | | | | | | | | | | |
| AAG | AGG | GAG | CTG | TGG | CCA | CCT | GAG | AAG | CTT | 260 |
| Lys | Arg | Glu | Leu | Trp | Pro | Pro | Glu | Lys | Leu | |
| 40 45 50 | | | | | | | | | | |
| AAA | GAG | AGG | TTA | CGG | AAG | CGG | CGG | GAG | GAG | 308 |
| Lys | Glu | Arg | Leu | Arg | Lys | Arg | Arg | Glu | Glu | |
| 55 60 65 | | | | | | | | | | |
| CAG | CAG | AAC | TCC | TGAGGCCTCC | AAGTGGGAGT | CCTAGCCCCCT | | | | 350 |
| Gln Gln Asn Ser | | | | | | | | | | |
| 70 | | | | | | | | | | |
| CCCCTGATGA | AATATACATA | TACTCAGTTC | CTTGTTATTC | | | | | | | 390 |

Sequence No.: 25

Sequence length: 4667

Sequence type: Nucleic acid

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Lymphoma

104

Cell line: U937

Clone name: HP10269

Sequence characteristics:

Code representing characteristics: CDS

Existence site: 754.. 4272

Characterization method: E

Sequence description

CATTAGTTA CTCTGCTCAT TTCTCTTAAG CTTTCCTTGG ATGAGTTGAG CTTTGAATCC 60
 TTCCTGATGA ACCTTGCCCTT TTAAGGATCC TCCAAATGCC CCAAGAAGCT GGGATTTTTC 120
 ATTTTTTTTT TCACTGGGGA GGGGAATGGT GCTTTCCAGG GTCCTGGATG TTTGAGTCTT 180
 CTCACCTTCC AGCCCGGTGA TATGTCTGGA GCTTTAACTC TCTATATAAG CCCTAATCTT 240
 TGTGTTCTCT GCCTGATCTT CTGTCTGGGG TGGTCCAGGT CACAAGAAGA AGCTGACCCC 300
 TGCTGGCTTT GGGAAAATGC TGAGTTCATT GCCTGGCACA AATGCAAGGG CCCTTCCCCA 360
 CCCTGTGAAT TCTGGTCTCT GATGATCACT TACATGTGCC TTGTGCTTTC TGTTTGAGGG 420
 GCCCCTTGCA GCCCCACAG GCAGGTGGGC ATTGTGGAGC TCACTACAAG AACTCTGGGA 480
 CCGACCGACC AACCCACTTG CCCAGTCCCG TCCTGGGAGG TGGGGGTGCA GTGACGACAG 540
 ATGGGTGTGA CGGCTGCCAG ATTCCTGAGA CCCGCCCTGC GGTGGGGCTA CACCCAGCCA 600
 GGGAGTCTCC AGAGGTGAGG CTGTTGTTTA AAAACCTGGA GCCGGGAGGG GAGACCCCCA 660
 CATTCAAGAG GAGCTTTCAG GCGATCTGGA GAAAGAACGG CAGAACACAC AGCAAGGAAA 720
 GGTCTTTTCT GGGGATCACC CCATTGGCTG AAG ATG AGA CCA TTC TTC CTC TTG 774

Met Arg Pro Phe Phe Leu Leu

1

5

TGT TTT GCC CTG CCT GGC CTC CTG CAT GCC CAA CAA GCC TGC TCC CGT 822

Cys Phe Ala Leu Pro Gly Leu Leu His Ala Gln Gln Ala Cys Ser Arg

10

15

20

GGG GCC TGC TAT CCA CCT GTT GGG GAC CTG CTT GTT GGG AGG ACC CGG 870

Gly Ala Cys Tyr Pro Pro Val Gly Asp Leu Leu Val Gly Arg Thr Arg

25

30

35

TTT CTC CGA GCT TCA TCT ACC TGT GGA CTG ACC AAG CCT GAG ACC TAC 918

0 1 2 3 4 5 6 7 8 9
 10 11 12 13 14 15 16 17 18 19
 20 21 22 23 24 25 26 27 28 29
 30 31 32 33 34 35 36 37 38 39
 40 41 42 43 44 45 46 47 48 49
 50 51 52 53 54 55 56 57 58 59
 60 61 62 63 64 65 66 67 68 69
 70 71 72 73 74 75 76 77 78 79
 80 81 82 83 84 85 86 87 88 89
 90 91 92 93 94 95 96 97 98 99

105

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|--|
| Phe | Leu | Arg | Ala | Ser | Ser | Thr | Cys | Gly | Leu | Thr | Lys | Pro | Glu | Thr | Tyr | | |
| 40 | | | | | 45 | | | | | 50 | | | | | 55 | | |
| TGC | ACC | CAG | TAT | GGC | GAG | TGG | CAG | ATG | AAA | TGC | TGC | AAG | TGT | GAC | TCC | 966 | |
| Cys | Thr | Gln | Tyr | Gly | Glu | Trp | Gln | Met | Lys | Cys | Cys | Lys | Cys | Asp | Ser | | |
| | | | | 60 | | | | | 65 | | | | | | 70 | | |
| AGG | CAG | CCT | CAC | AAC | TAC | TAC | AGT | CAC | CGA | GTA | GAG | AAT | GTG | GCT | TCA | 1014 | |
| Arg | Gln | Pro | His | Asn | Tyr | Tyr | Ser | His | Arg | Val | Glu | Asn | Val | Ala | Ser | | |
| | | | | 75 | | | | | 80 | | | | | | 85 | | |
| TCC | TCC | GGC | CCC | ATG | CGC | TGG | TGG | CAG | TCC | CAG | AAT | GAT | GTG | AAC | CCT | 1062 | |
| Ser | Ser | Gly | Pro | Met | Arg | Trp | Trp | Gln | Ser | Gln | Asn | Asp | Val | Asn | Pro | | |
| | | | | 90 | | | | | 95 | | | | | | 100 | | |
| GTC | TCT | CTG | CAG | CTG | GAC | CTG | GAC | AGG | AGA | TTC | CAG | CTT | CAA | GAA | GTC | 1110 | |
| Val | Ser | Leu | Gln | Leu | Asp | Leu | Asp | Arg | Arg | Phe | Gln | Leu | Gln | Glu | Val | | |
| | | | | 105 | | | | | 110 | | | | | | 115 | | |
| ATG | ATG | GAG | TTC | CAG | GGG | CCC | ATG | CCT | GCC | GGC | ATG | CTG | ATT | GAG | CGC | 1158 | |
| Met | Met | Glu | Phe | Gln | Gly | Pro | Met | Pro | Ala | Gly | Met | Leu | Ile | Glu | Arg | | |
| | | | | | | | | | | | | | | | | | |
| 120 | | | | | 125 | | | | | 130 | | | | | 135 | | |
| TCC | TCA | GAC | TTC | GGT | AAG | ACC | TGG | CGA | GTG | TAC | CAG | TAC | CTG | GCT | GCC | 1206 | |
| Ser | Ser | Asp | Phe | Gly | Lys | Thr | Trp | Arg | Val | Tyr | Gln | Tyr | Leu | Ala | Ala | | |
| | | | | | | | | | | | | | | | | | |
| | | | | 140 | | | | | 145 | | | | | | 150 | | |
| GAC | TGC | ACC | TCC | ACC | TTC | CCT | CGG | GTC | CGC | CAG | GGT | CGG | CCT | CAG | AGC | 1254 | |
| Asp | Cys | Thr | Ser | Thr | Phe | Pro | Arg | Val | Arg | Gln | Gly | Arg | Pro | Gln | Ser | | |
| | | | | | | | | | | | | | | | | | |
| | | | | 155 | | | | | 160 | | | | | | 165 | | |
| TGG | CAG | GAT | GTT | CGG | TGC | CAG | TCC | CTG | CCT | CAG | AGG | CCT | AAT | GCA | CGC | 1302 | |
| Trp | Gln | Asp | Val | Arg | Cys | Gln | Ser | Leu | Pro | Gln | Arg | Pro | Asn | Ala | Arg | | |
| | | | | | | | | | | | | | | | | | |
| | | | | 170 | | | | | 175 | | | | | | 180 | | |
| CTA | AAT | GGG | GGG | AAG | GTC | CAA | CTT | AAC | CTT | ATG | GAT | TTA | GTG | TCT | GGG | 1350 | |
| Leu | Asn | Gly | Gly | Lys | Val | Gln | Leu | Asn | Leu | Met | Asp | Leu | Val | Ser | Gly | | |
| | | | | | | | | | | | | | | | | | |
| | | | | 185 | | | | | 190 | | | | | | 195 | | |

09254750-041599

106

ATT CCA GCA ACT CAA AGT CAA AAA ATT CAA GAG GTG GGG GAG ATC ACA 1398
 Ile Pro Ala Thr Gln Ser Gln Lys Ile Gln Glu Val Gly Glu Ile Thr
 200 205 210 215
 AAC TTG AGA GTC AAT TTC ACC AGG CTG GCC CCT GTG CCC CAA AGG GGC 1446
 Asn Leu Arg Val Asn Phe Thr Arg Leu Ala Pro Val Pro Gln Arg Gly
 220 225 230
 TAC CAC CCT CCC AGC GCC TAC TAT GCT GTG TCC CAG CTC CGT CTG CAG 1494
 Tyr His Pro Pro Ser Ala Tyr Tyr Ala Val Ser Gln Leu Arg Leu Gln
 235 240 245
 GGG AGC TGC TTC TGT CAC GGC CAT GCT GAT CGC TGC GCA CCC AAG CCT 1542
 Gly Ser Cys Phe Cys His Gly His Ala Asp Arg Cys Ala Pro Lys Pro
 250 255 260
 GGG GCC TCT GCA GGC CCC TCC ACC GCT GTG CAG GTC CAC GAT GTC TGT 1590
 Gly Ala Ser Ala Gly Pro Ser Thr Ala Val Gln Val His Asp Val Cys
 265 270 275
 GTC TGC CAG CAC AAC ACT GCC GGC CCA AAT TGT GAG CGC TGT GCA CCC 1638
 Val Cys Gln His Asn Thr Ala Gly Pro Asn Cys Glu Arg Cys Ala Pro
 280 285 290 295
 TTC TAC AAC AAC CGG CCC TGG AGA CCG GCG GAG GGC CAG GAC GCC CAT 1686
 Phe Tyr Asn Asn Arg Pro Trp Arg Pro Ala Glu Gly Gln Asp Ala His
 300 305 310
 GAA TGC CAA AGG TGC GAC TGC AAT GGG CAC TCA GAG ACA TGT CAC TTT 1734
 Glu Cys Gln Arg Cys Asp Cys Asn Gly His Ser Glu Thr Cys His Phe
 315 320 325
 GAC CCC GCT GTG TTT GCC GCC AGC CAG GGG GCA TAT GGA GGT GTG TGT 1782
 Asp Pro Ala Val Phe Ala Ala Ser Gln Gly Ala Tyr Gly Gly Val Cys
 330 335 340
 GAC AAT TGC CGG GAC CAC ACC GAA GGC AAG AAC TGT GAG CGG TGT CAG 1830
 Asp Asn Cys Arg Asp His Thr Glu Gly Lys Asn Cys Glu Arg Cys Gln

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| | | | |
|---|-----|-----|------|
| 345 | 350 | 355 | |
| CTG CAC TAT TTC CGG AAC CGG CGC CCG GGA GCT TCC ATT CAG GAG ACC | | | 1878 |
| Leu His Tyr Phe Arg Asn Arg Arg Pro Gly Ala Ser Ile Gln Glu Thr | | | |
| 360 | 365 | 370 | 375 |
| TGC ATC TCC TGC GAG TGT GAT CCG GAT GGG GCA GTG CCA GGG GCT CCC | | | 1926 |
| Cys Ile Ser Cys Glu Cys Asp Pro Asp Gly Ala Val Pro Gly Ala Pro | | | |
| | 380 | 385 | 390 |
| TGT GAC CCA GTG ACC GGG CAG TGT GTG TGC AAG GAG CAT GTG CAG GGA | | | 1974 |
| Cys Asp Pro Val Thr Gly Gln Cys Val Cys Lys Glu His Val Gln Gly | | | |
| | 395 | 400 | 405 |
| GAG CGC TGT GAC CTA TGC AAG CCG GGC TTC ACT GGA CTC ACC TAC GCC | | | 2022 |
| Glu Arg Cys Asp Leu Cys Lys Pro Gly Phe Thr Gly Leu Thr Tyr Ala | | | |
| | 410 | 415 | 420 |
| AAC CCG CAG GGC TGC CAC CGC TGT GAC TGC AAC ATC CTG GGG TCC CGG | | | 2070 |
| Asn Pro Gln Gly Cys His Arg Cys Asp Cys Asn Ile Leu Gly Ser Arg | | | |
| | 425 | 430 | 435 |
| AGG GAC ATG CCG TGT GAC GAG GAG AGT GGG CGC TGC CTT TGT CTG CCC | | | 2118 |
| Arg Asp Met Pro Cys Asp Glu Glu Ser Gly Arg Cys Leu Cys Leu Pro | | | |
| | 440 | 445 | 450 |
| AAC GTG GTG GGT CCC AAA TGT GAC CAG TGT GCT CCC TAC CAC TGG AAG | | | 2166 |
| Asn Val Val Gly Pro Lys Cys Asp Gln Cys Ala Pro Tyr His Trp Lys | | | |
| | 460 | 465 | 470 |
| CTG GCC AGT GGC CAG GGC TGT GAA CCG TGT GCC TGC GAC CCG CAC AAC | | | 2214 |
| Leu Ala Ser Gly Gln Gly Cys Glu Pro Cys Ala Cys Asp Pro His Asn | | | |
| | 475 | 480 | 485 |
| TCC CTC AGC CCA CAG TGC AAC CAG TTC ACA GGG CAG TGC CCC TGT CGG | | | 2262 |
| Ser Leu Ser Pro Gln Cys Asn Gln Phe Thr Gly Gln Cys Pro Cys Arg | | | |
| | 490 | 495 | 500 |
| GAA GGC TTT GGT GGC CTG ATG TGC AGC GCT GCA GCC ATC CGC CAG TGT | | | 2310 |

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| | |
|---|------|
| Glu Gly Phe Gly Gly Leu Met Cys Ser Ala Ala Ala Ile Arg Gln Cys | |
| 505 | 510 |
| CCA GAC CGG ACC TAT GGA GAC GTG GCC ACA GGA TGC CGA GCC TGT GAC | 2358 |
| Pro Asp Arg Thr Tyr Gly Asp Val Ala Thr Gly Cys Arg Ala Cys Asp | |
| 520 | 525 |
| TGT GAT TTC CGG GGA ACA GAG GGC CCG GGC TGC GAC AAG GCA TCA GGC | 2406 |
| Cys Asp Phe Arg Gly Thr Glu Gly Pro Gly Cys Asp Lys Ala Ser Gly | |
| 540 | 545 |
| CGC TGC CTC TGC CGC CCT GGC TTG ACC GGG CCC CGC TGT GAC CAG TGC | 2454 |
| Arg Cys Leu Cys Arg Pro Gly Leu Thr Gly Pro Arg Cys Asp Gln Cys | |
| 555 | 560 |
| CAG CGA GGC TAC TGC AAT CGC TAC CCG GTG TGC GTG GCC TGC CAC CCT | 2502 |
| Gln Arg Gly Tyr Cys Asn Arg Tyr Pro Val Cys Val Ala Cys His Pro | |
| 570 | 575 |
| TGC TTC CAG ACC TAT GAT GCG GAC CTC CGG GAG CAG GCC CTG CGC TTT | 2550 |
| Cys Phe Gln Thr Tyr Asp Ala Asp Leu Arg Glu Gln Ala Leu Arg Phe | |
| 585 | 590 |
| GGT AGA CTC CGC AAT GCC ACC GCC AGC CTG TGG TCA GGG CCT GGG CTG | 2598 |
| Gly Arg Leu Arg Asn Ala Thr Ala Ser Leu Trp Ser Gly Pro Gly Leu | |
| 600 | 605 |
| GAG GAC CGT GGC CTG GCC TCC CGG ATC CTA GAT GCA AAG AGT AAG ATT | 2646 |
| Glu Asp Arg Gly Leu Ala Ser Arg Ile Leu Asp Ala Lys Ser Lys Ile | |
| 620 | 625 |
| GAG CAG ATC CGA GCA GTT CTC AGC AGC CCC GCA GTC ACA GAG CAG GAG | 2694 |
| Glu Gln Ile Arg Ala Val Leu Ser Ser Pro Ala Val Thr Glu Gln Glu | |
| 635 | 640 |
| GTG GCT CAG GTG GCC AGT GCC ATC CTC TCC CTC AGG CGA ACT CTC CAG | 2742 |
| Val Ala Gln Val Ala Ser Ala Ile Leu Ser Leu Arg Arg Thr Leu Gln | |
| 650 | 655 |
| | 660 |

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GGC CTG CAG CTG GAT CTG CCC CTG GAG GAG GAG ACG TTG TCC CTT CCG 2790
Gly Leu Gln Leu Asp Leu Pro Leu Glu Glu Glu Thr Leu Ser Leu Pro
665 670 675

AGA GAC CTG GAG AGT CTT GAC AGA AGC TTC AAT GGT CTC CTT ACT ATG 2838
Arg Asp Leu Glu Ser Leu Asp Arg Ser Phe Asn Gly Leu Leu Thr Met
680 685 690 695

TAT CAG AGG AAG AGG GAG CAG TTT GAA AAA ATA AGC AGT GCT GAT CCT 2886
Tyr Gln Arg Lys Arg Glu Gln Phe Glu Lys Ile Ser Ser Ala Asp Pro
700 705 710

TCA GGA GCC TTC CGG ATG CTG AGC ACA GCC TAC GAG CAG TCA GCC CAG 2934
Ser Gly Ala Phe Arg Met Leu Ser Thr Ala Tyr Glu Gln Ser Ala Gln
715 720 725

GCT GCT CAG CAG GTC TCC GAC AGC TCG CGC CTT TTG GAC CAG CTC AGG 2982
Ala Ala Gln Gln Val Ser Asp Ser Ser Arg Leu Leu Asp Gln Leu Arg
730 735 740

GAC AGC CGG AGA GAG GCA GAG AGG CTG GTG CGG CAG GCG GGA GGA GGA 3030
Asp Ser Arg Arg Glu Ala Glu Arg Leu Val Arg Gln Ala Gly Gly Gly
745 750 755

GGA GGC ACC GGC AGC CCC AAG CTT GTG GCC CTG AGG CTG GAG ATG TCT 3078
Gly Gly Thr Gly Ser Pro Lys Leu Val Ala Leu Arg Leu Glu Met Ser
760 765 770 775

TCG TTG CCT GAC CTG ACA CCC ACC TTC AAC AAG CTC TGT GGC AAC TCC 3126
Ser Leu Pro Asp Leu Thr Pro Thr Phe Asn Lys Leu Cys Gly Asn Ser
780 785 790

AGG CAG ATG GCT TGC ACC CCA ATA TCA TGC CCT GGT GAG CTA TGT CCC 3174
Arg Gln Met Ala Cys Thr Pro Ile Ser Cys Pro Gly Glu Leu Cys Pro
795 800 805

CAA GAC AAT GGC ACA GCC TGT GGC TCC CGC TGC AGG GGT GTC CTT CCC 3222
Gln Asp Asn Gly Thr Ala Cys Gly Ser Arg Cys Arg Gly Val Leu Pro

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110

| | | | |
|---|-----|-----|------|
| 810 | 815 | 820 | |
| AGG GCC GGT GGG GCC TTC TTG ATG GCG GGG CAG GTG GCT GAG CAG CTG | | | 3270 |
| Arg Ala Gly Gly Ala Phe Leu Met Ala Gly Gln Val Ala Glu Gln Leu | | | |
| 825 | 830 | 835 | |
| CGG GGC TTC AAT GCC CAG CTC CAG CGG ACC AGG CAG ATG ATT AGG GCA | | | 3318 |
| Arg Gly Phe Asn Ala Gln Leu Gln Arg Thr Arg Gln Met Ile Arg Ala | | | |
| 840 | 845 | 850 | 855 |
| GCC GAG GAA TCT GCC TCA CAG ATT CAA TCC AGT GCC CAG CGC TTG GAG | | | 3366 |
| Ala Glu Glu Ser Ala Ser Gln Ile Gln Ser Ser Ala Gln Arg Leu Glu | | | |
| 860 | 865 | 870 | |
| ACC CAG GTG AGC GCC AGC CGC TCC CAG ATG GAG GAA GAT GTC AGA CGC | | | 3414 |
| Thr Gln Val Ser Ala Ser Arg Ser Gln Met Glu Glu Asp Val Arg Arg | | | |
| 875 | 880 | 885 | |
| ACA CGG CTC CTA ATC CAG CAG GTC CGG GAC TTC CTA ACA GAC CCC GAC | | | 3462 |
| Thr Arg Leu Leu Ile Gln Gln Val Arg Asp Phe Leu Thr Asp Pro Asp | | | |
| 890 | 895 | 900 | |
| ACT GAT GCA GCC ACT ATC CAG GAG GTC AGC GAG GCC GTG CTG GCC CTG | | | 3510 |
| Thr Asp Ala Ala Thr Ile Gln Glu Val Ser Glu Ala Val Leu Ala Leu | | | |
| 905 | 910 | 915 | |
| TGG CTG CCC ACA GAC TCA GCT ACT GTT CTG CAG AAG ATG AAT GAG ATC | | | 3558 |
| Trp Leu Pro Thr Asp Ser Ala Thr Val Leu Gln Lys Met Asn Glu Ile | | | |
| 920 | 925 | 930 | 935 |
| CAG GCC ATT GCA GCC AGG CTC CCC AAC GTG GAC TTG GTG CTG TCC CAG | | | 3606 |
| Gln Ala Ile Ala Ala Arg Leu Pro Asn Val Asp Leu Val Leu Ser Gln | | | |
| 940 | 945 | 950 | |
| ACC AAG CAG GAC ATT GCG CGT GCC CGC CGG TTG CAG GCT GAG GCT GAG | | | 3654 |
| Thr Lys Gln Asp Ile Ala Arg Ala Arg Arg Leu Gln Ala Glu Ala Glu | | | |
| 955 | 960 | 965 | |
| GAA GCC AGG AGC CGA GCC CAT GCA GTG GAG GGC CAG GTG GAA GAT GTG | | | 3702 |

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| | | | | | | | | | | | | | | | | |
|---|--|--|--|------|--|--|--|------|--|--|--|------|--|--|--|------|
| Glu Ala Arg Ser Arg Ala His Ala Val Glu Gly Gln Val Glu Asp Val | | | | | | | | | | | | | | | | |
| 970 | | | | 975 | | | | 980 | | | | | | | | |
| GTT GGG AAC CTG CGG CAG GGG ACA GTG GCA CTG CAG GAA GCT CAG GAC | | | | | | | | | | | | | | | | 3750 |
| Val Gly Asn Leu Arg Gln Gly Thr Val Ala Leu Gln Glu Ala Gln Asp | | | | | | | | | | | | | | | | |
| 985 | | | | 990 | | | | 995 | | | | | | | | |
| ACC ATG CAA GGC ACC AGC CGC TCC CTT CGG CTT ATC CAG GAC AGG GTT | | | | | | | | | | | | | | | | 3798 |
| Thr Met Gln Gly Thr Ser Arg Ser Leu Arg Leu Ile Gln Asp Arg Val | | | | | | | | | | | | | | | | |
| 1000 | | | | 1005 | | | | 1010 | | | | 1015 | | | | |
| GCT GAG GTT CAG CAG GTA CTG CGG CCA GCA GAA AAG CTG GTG ACA AGC | | | | | | | | | | | | | | | | 3846 |
| Ala Glu Val Gln Gln Val Leu Arg Pro Ala Glu Lys Leu Val Thr Ser | | | | | | | | | | | | | | | | |
| | | | | 1020 | | | | 1025 | | | | 1030 | | | | |
| ATG ACC AAG CAG CTG GGT GAC TTC TGG ACA CGG ATG GAG GAG CTC CGC | | | | | | | | | | | | | | | | 3894 |
| Met Thr Lys Gln Leu Gly Asp Phe Trp Thr Arg Met Glu Glu Leu Arg | | | | | | | | | | | | | | | | |
| | | | | 1035 | | | | 1040 | | | | 1045 | | | | |
| CAC CAA GCC CGG CAG CAG GGG GCA GAG GCA GTC CAG GCC CAG CAG CTT | | | | | | | | | | | | | | | | 3942 |
| His Gln Ala Arg Gln Gln Gly Ala Glu Ala Val Gln Ala Gln Gln Leu | | | | | | | | | | | | | | | | |
| 1050 | | | | 1055 | | | | 1060 | | | | | | | | |
| GCG GAA GGT GCC AGC GAG CAG GCA TTG AGT GCC CAA GAG GGA TTT GAG | | | | | | | | | | | | | | | | 3990 |
| Ala Glu Gly Ala Ser Glu Gln Ala Leu Ser Ala Gln Glu Gly Phe Glu | | | | | | | | | | | | | | | | |
| 1065 | | | | 1070 | | | | 1075 | | | | | | | | |
| AGA ATA AAA CAA AAG TAT GCT GAG TTG AAG GAC CGG TTG GGT CAG AGT | | | | | | | | | | | | | | | | 4038 |
| Arg Ile Lys Gln Lys Tyr Ala Glu Leu Lys Asp Arg Leu Gly Gln Ser | | | | | | | | | | | | | | | | |
| 1080 | | | | 1085 | | | | 1090 | | | | 1095 | | | | |
| TCC ATG CTG GGT GAG CAG GGT GCC CGG ATC CAG AGT GTG AAG ACA GAG | | | | | | | | | | | | | | | | 4086 |
| Ser Met Leu Gly Glu Gln Gly Ala Arg Ile Gln Ser Val Lys Thr Glu | | | | | | | | | | | | | | | | |
| | | | | 1100 | | | | 1105 | | | | 1110 | | | | |
| GCA GAG GAG CTG TTT GGG GAG ACC ATG GAG ATG ATG GAC AGG ATG AAA | | | | | | | | | | | | | | | | 4134 |
| Ala Glu Glu Leu Phe Gly Glu Thr Met Glu Met Met Asp Arg Met Lys | | | | | | | | | | | | | | | | |
| 1115 | | | | 1120 | | | | 1125 | | | | | | | | |

1130

1140

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1165

1170

Sequence No. : 26

Sequence length: 1086

Sequence type: Nucleic acid

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Stomach cancer

Clone name: HP10298

Sequence characteristics:

Code representing characteristics: CDS

113

Existence site: 138.. 506

Characterization method: E

Sequence description

TTTAATTTCC CCGAAATCAG ACTGCTGCCT TGGACCGGGA CAGCTCGCGG CCCCCGAGAG 60
CTCTAGCCGT CGAGGAGCTG CCTGGGGACG TTTGCCCTGG GGCCCCAGCC TGGCCCGGGT 120
CACCTGGCA TGAGGAG ATG GGC CTG TTG CTC CTG GTC CCA TTG CTC CTG 170
Met Gly Leu Leu Leu Leu Val Pro Leu Leu Leu
1 5 10
CTG CCC GGC TCC TAC GGA CTG CCC TTC TAC AAC GGC TTC TAC TAC TCC 218
Leu Pro Gly Ser Tyr Gly Leu Pro Phe Tyr Asn Gly Phe Tyr Tyr Ser
15 20 25
AAC AGC GCC AAC GAC CAG AAC CTA GGC AAC GGT CAT GGC AAA GAC CTC 266
Asn Ser Ala Asn Asp Gln Asn Leu Gly Asn Gly His Gly Lys Asp Leu
30 35 40
CTT AAT GGA GTG AAG CTG GTG GTG GAG ACA CCC GAG GAG ACC CTG TTC 314
Leu Asn Gly Val Lys Leu Val Val Glu Thr Pro Glu Glu Thr Leu Phe
45 50 55
ACC CGC ATC CTA ACT GTG GGC CCC CAG AGC CTG GGG TCC GAA GCT TTG 362
Thr Arg Ile Leu Thr Val Gly Pro Gln Ser Leu Gly Ser Glu Ala Leu
60 65 70 75
GCT TCC CCG ACC CGC AGA GCC GCT TGT ACG GTG TTT ACT GCT ACC GCC 410
Ala Ser Pro Thr Arg Arg Ala Ala Cys Thr Val Phe Thr Ala Thr Ala
80 85 90
AGC ACT AGG ACC TGG GGC CCT CCC CTG CCG CAT TCC CTC ACT GGC TGT 458
Ser Thr Arg Thr Trp Gly Pro Pro Leu Pro His Ser Leu Thr Gly Cys
95 100 105
GTA TTT ATT GAG TGG TTC GTT TTC CCT TGT GGG TTG GAG CCA TTT 503
Val Phe Ile Glu Trp Phe Val Phe Pro Cys Gly Leu Glu Pro Phe
110 115 120

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114

TAACGTGTTTATACCTTCTCAATTTAAATTTTCTTTAACATTTTTTTTACTATTTTT560
TGTAAGCAAACAGAACCCAATGCCTCCCTTTGCTCCTGGATGCCCCACTCCAGGAATCA620
TGCTTGCTCCCTGGGGCCATTTGCGGTTTTGTGGGCTTCTGGAGGGTTCCCGCCATCCA680
GGCTGGTCTCCCTCCCTTAAAGAGGTTGGTCCCCAGAGTGGCGGTGGCCGTCTAGAAT740
GCCGCCGGGAGTCCGGGCATGGTGGGCACAGTTCTCCCTGCCCCTCAGCCTGGGGGAAGA800
AGAGGGCCTCGGGGGCCTCCGGAGCTGGGC TTGGGGCCTCTCCTGCCACCTCTACTTCT860
CTGTGAAGCCGCTGACCCCA GTCTGCCAC TGAGGGGCTAGGGCTGGAAGCCAGTTCTAG920
GCTTCCAGGC GAAAGCTGAGGGAAGGAAGA AACTCCCCTCCCCGTTCCCC TTCCCCTCTC980
GGTTCCAAAG AATCTGTTTT GTTGTCATTT GTTTCTCCTGTTCCCTGTGTGGGGAGGGG1040
CCCTCAGGTG TGTGTACTTT GGACAATAAA TGGTGCTATG ACTGCC1086

Sequence No.: 27

Sequence length: 866

Sequence type: Nucleic acid

Strandedness: Double

Topology: Linear

Sequence kind: cDNA to mRNA

Original source:

Organism species: *Homo sapiens*

Cell kind: Stomach cancer

Clone name: HP10368

Sequence characteristics:

Code representing characteristics: CDS

Existence site: 73.. 600

Characterization method: E

Sequence description

ACTCAGAAGC TTGGACCGCA TCCTAGCCGC GACTCACAC AAGGCAGGTG GGTGAGGAAA60
TCCAGAGTTG CC ATG GAG AAA ATT CCA GTG TCA GCA TTC TTG CTC CTT GTG111

Met Glu Lys Ile Pro Val Ser Ala Phe Leu Leu Leu Val

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| | | | | | | | | | | | | | | | 1 | | | | | | 5 | | | | | | 10 | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|-----|--|--|-----|----|--|--|--|-----|--|----|--|--|-----|--|--|----|--|--|
| GCC | CTC | TCC | TAC | ACT | CTG | GCC | AGA | GAT | ACC | ACA | GTC | AAA | CCT | GGA | GCC | | 159 | | | | | | | | | | | | | | | | | | |
| Ala | Leu | Ser | Tyr | Thr | Leu | Ala | Arg | Asp | Thr | Thr | Val | Lys | Pro | Gly | Ala | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | 15 | | | | | | 20 | | | | | | 25 | | | | | | | | |
| AAA | AAG | GAC | ACA | AAG | GAC | TCT | CGA | CCC | AAA | CTG | CCC | CAG | ACC | CTC | TCC | | 207 | | | | | | | | | | | | | | | | | | |
| Lys | Lys | Asp | Thr | Lys | Asp | Ser | Arg | Pro | Lys | Leu | Pro | Gln | Thr | Leu | Ser | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | 30 | | | | | | 35 | | | | | | 40 | | | | | | 45 | | |
| AGA | GGT | TGG | GGT | GAC | CAA | CTC | ATC | TGG | ACT | CAG | ACA | TAT | GAA | GAA | GCT | | 255 | | | | | | | | | | | | | | | | | | |
| Arg | Gly | Trp | Gly | Asp | Gln | Leu | Ile | Trp | Thr | Gln | Thr | Tyr | Glu | Glu | Ala | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | 50 | | | | | 55 | | | | | 60 | | | | | | | | | | |
| CTA | TAT | AAA | TCC | AAG | ACA | AGC | AAC | AAA | CCC | TTG | ATG | ATT | ATT | CAT | CAC | | 303 | | | | | | | | | | | | | | | | | | |
| Leu | Tyr | Lys | Ser | Lys | Thr | Ser | Asn | Lys | Pro | Leu | Met | Ile | Ile | His | His | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | 65 | | | | | 70 | | | | | 75 | | | | | | | | | | |
| TTG | GAT | GAG | TGC | CCA | CAC | AGT | CAA | GCT | TTA | AAG | AAA | GTG | TTT | GCT | GAA | | 351 | | | | | | | | | | | | | | | | | | |
| Leu | Asp | Glu | Cys | Pro | His | Ser | Gln | Ala | Leu | Lys | Lys | Val | Phe | Ala | Glu | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | 80 | | | | | 85 | | | | | 90 | | | | | | | | | | |
| AAT | AAA | GAA | ATC | CAG | AAA | TTG | GCA | GAG | CAG | TTT | GTC | CTC | CTC | AAT | CTG | | 399 | | | | | | | | | | | | | | | | | | |
| Asn | Lys | Glu | Ile | Gln | Lys | Leu | Ala | Glu | Gln | Phe | Val | Leu | Leu | Asn | Leu | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | 95 | | | | | 100 | | | | | 105 | | | | | | | | | | |
| GTT | TAT | GAA | ACA | ACT | GAC | AAA | CAC | CTT | TCT | CCT | GAT | GGC | CAG | TAT | GTC | | 447 | | | | | | | | | | | | | | | | | | |
| Val | Tyr | Glu | Thr | Thr | Asp | Lys | His | Leu | Ser | Pro | Asp | Gly | Gln | Tyr | Val | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | 110 | | | | | 115 | | | | | 120 | | | | | 125 | | | | | |
| CCC | AGG | ATT | ATG | TTT | GTT | GAC | CCA | TCT | CTG | ACA | GTT | AGA | GCC | GAT | ATC | | 495 | | | | | | | | | | | | | | | | | | |
| Pro | Arg | Ile | Met | Phe | Val | Asp | Pro | Ser | Leu | Thr | Val | Arg | Ala | Asp | Ile | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | 130 | | | | | 135 | | | | | 140 | | | | | | | | | | |
| ACT | GGA | AGA | TAT | TCA | AAC | CGT | CTC | TAT | GCT | TAC | GAA | CCT | GCA | GAT | ACA | | 543 | | | | | | | | | | | | | | | | | | |
| Thr | Gly | Arg | Tyr | Ser | Asn | Arg | Leu | Tyr | Ala | Tyr | Glu | Pro | Ala | Asp | Thr | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | 145 | | | | | 150 | | | | | 155 | | | | | | | | | | |
| GCT | CTG | TTG | CTT | GAC | AAC | ATG | AAG | AAA | GCT | CTC | AAG | TTG | CTG | AAG | ACT | | 591 | | | | | | | | | | | | | | | | | | |

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Ala Leu Leu Leu Asp Asn Met Lys Lys Ala Leu Lys Leu Leu Lys Thr

160

165

170

GAA TTG TAAAGAAAAA AAATCTCCAA GCCCTTCTGT CTGTCAGGCC TTG

640

Glu Leu

175

AGACTTGAAA CCAGAAGAAG TGTGAGAAGA CTGGCTAGTG TGGAAGCATA GTGAACACAC

700

TGATTAGGTT ATGGTTTAAT GTTACAACAA CTATTTTTTA AGAAAAACAA GTTTTAGAAA

760

TTTGGTTTCA AGTGTACATG TGTGAAAACA ATATTGTATA CTACCATAGT GAGCCATGAT

820

TTTCTAAAAA AAAAAATAAA TGTTTTGGGG GTGTTCTGTT TTCTCC

866

099740-04169

Claims

1. Proteins containing any of the amino acid sequences represented by Sequence No. 1 to Sequence No. 9.
2. DNAs encoding any of the proteins as described in Claim 1.
3. cDNAs containing any of the base sequences represented by Sequence No. 10 to Sequence No. 18.
4. cDNAs described in Claim 3 which comprise any of the base sequences represented by Sequence No. 19 to Sequence No. 27.

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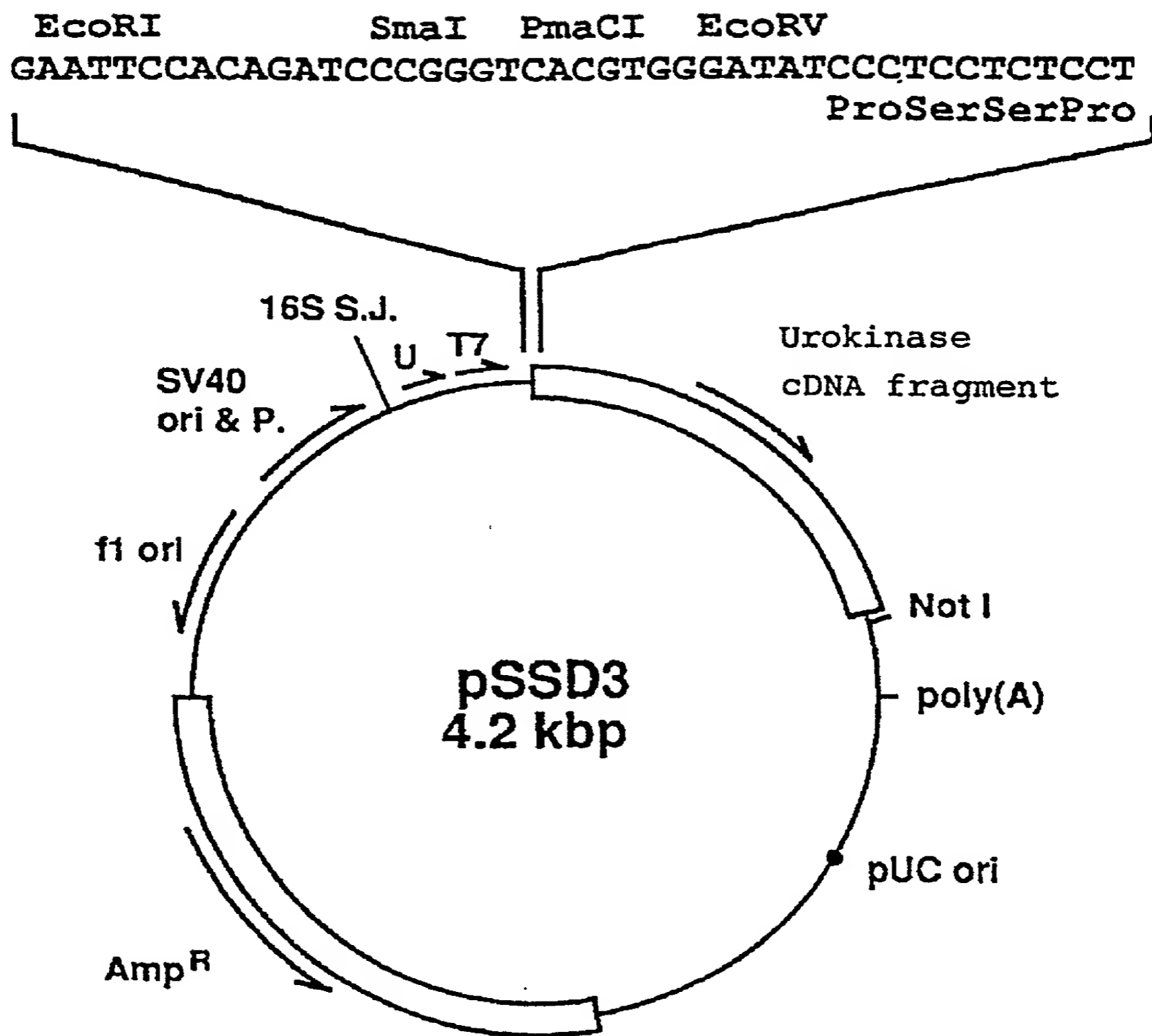
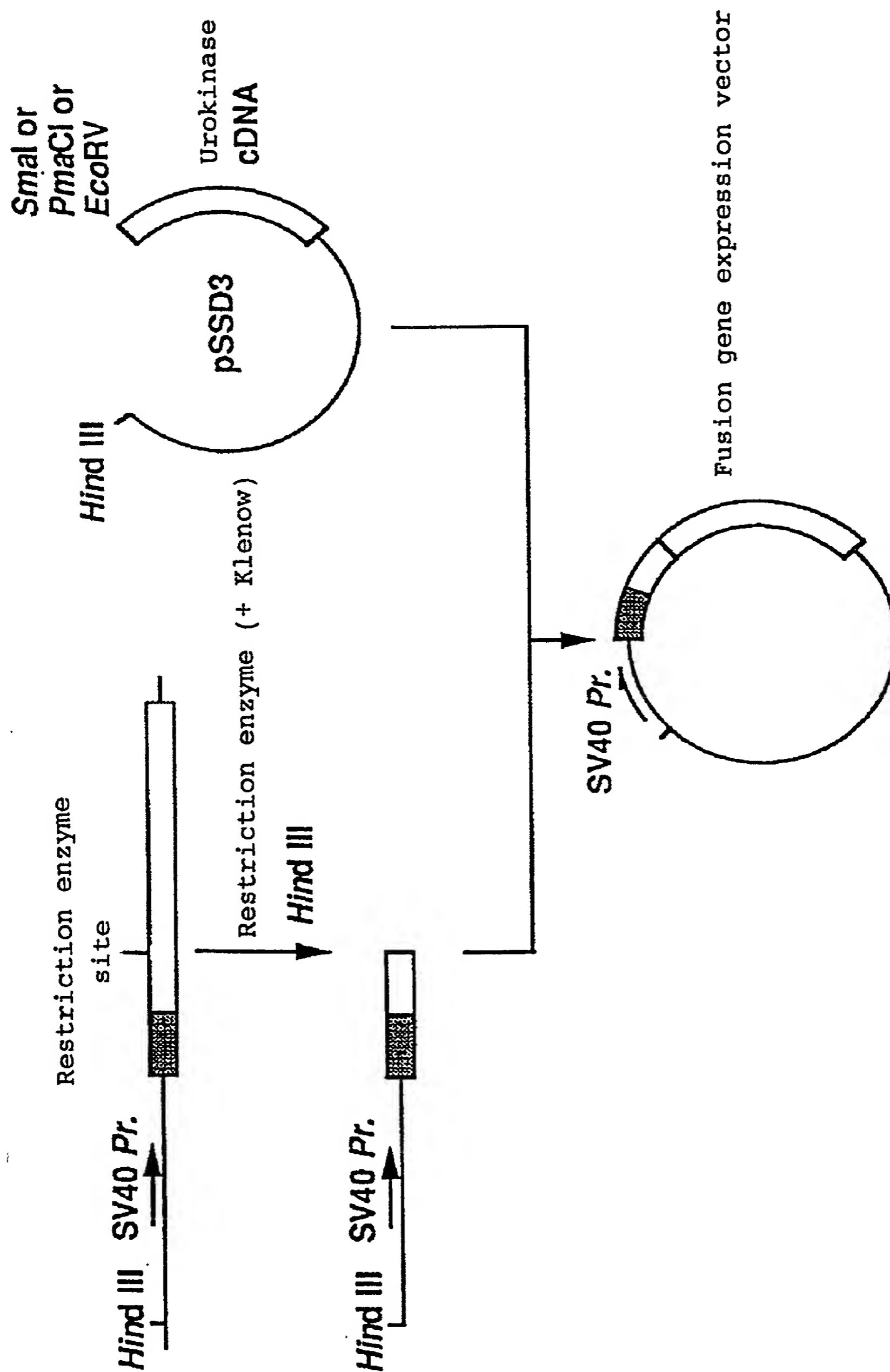


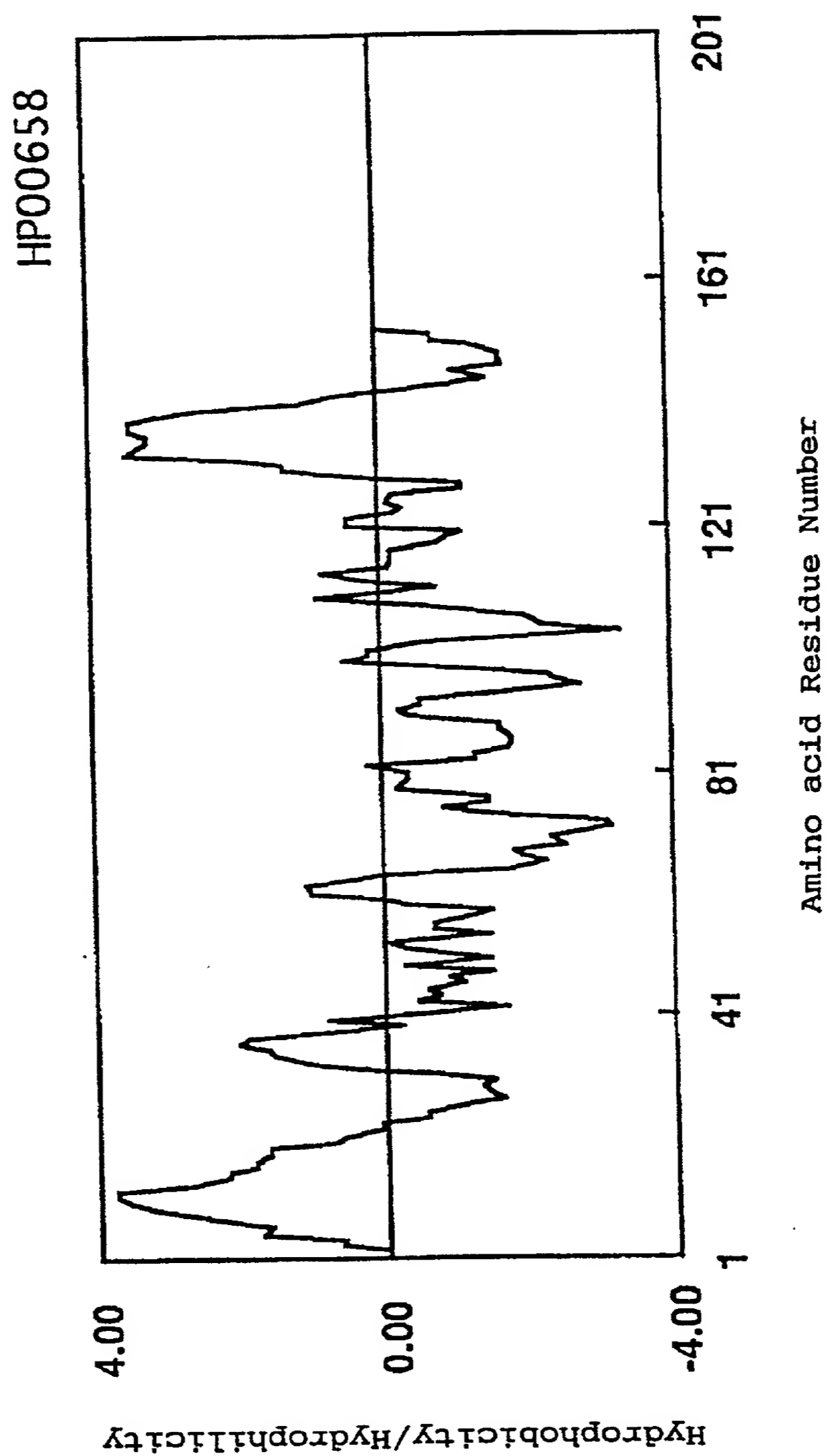
Fig.1

Fig. 2



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Fig. 3



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Fig. 4

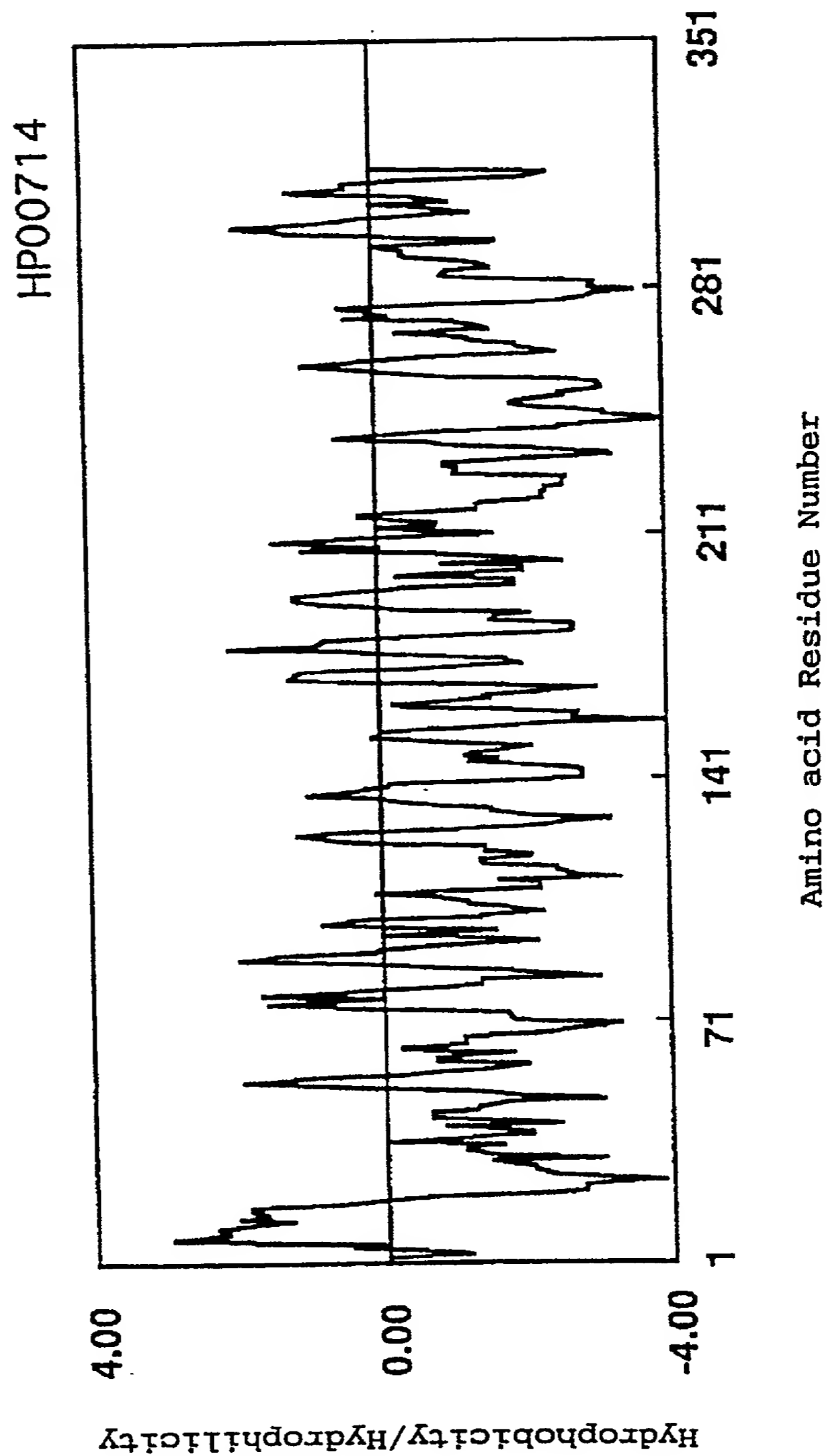
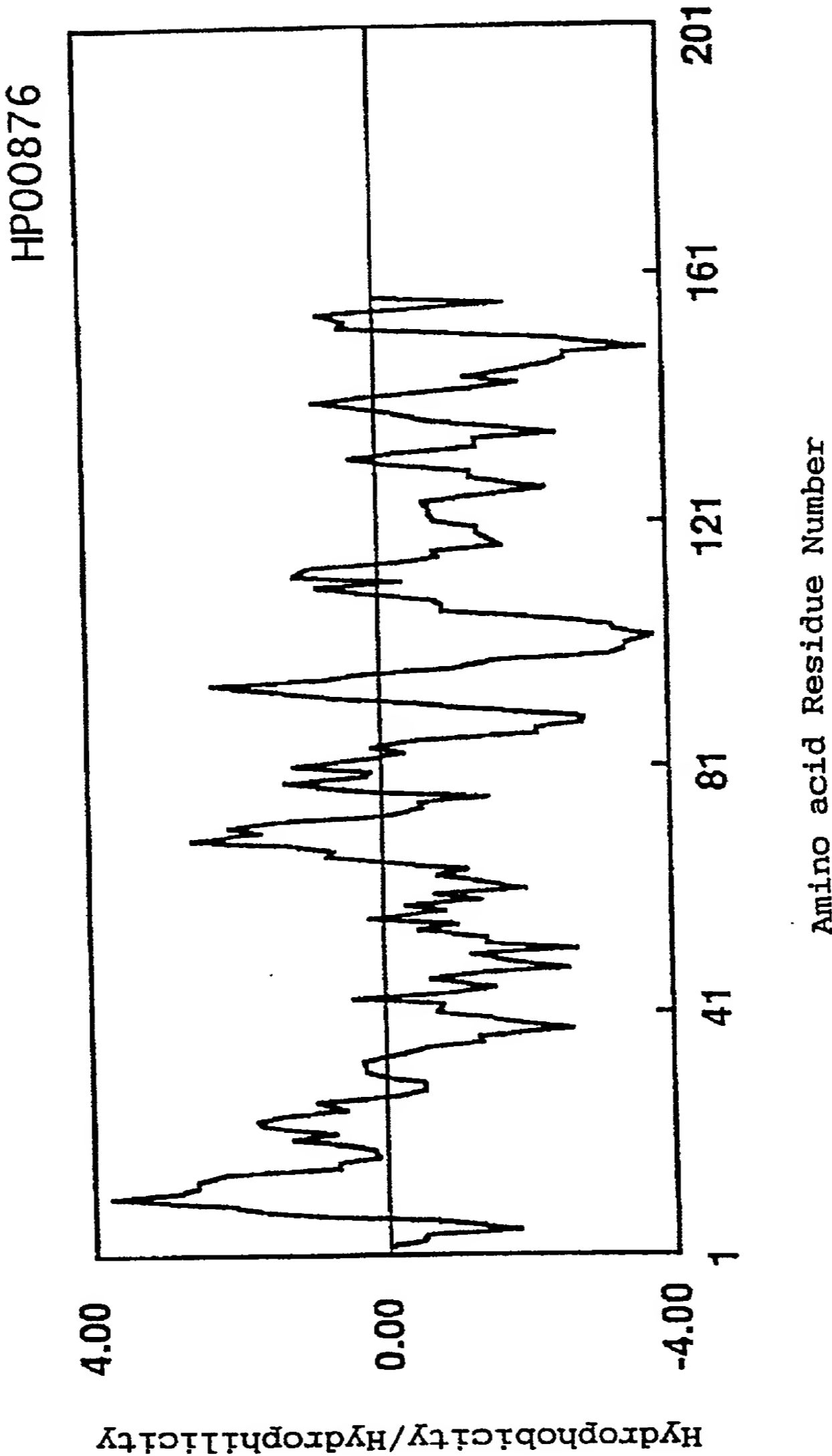
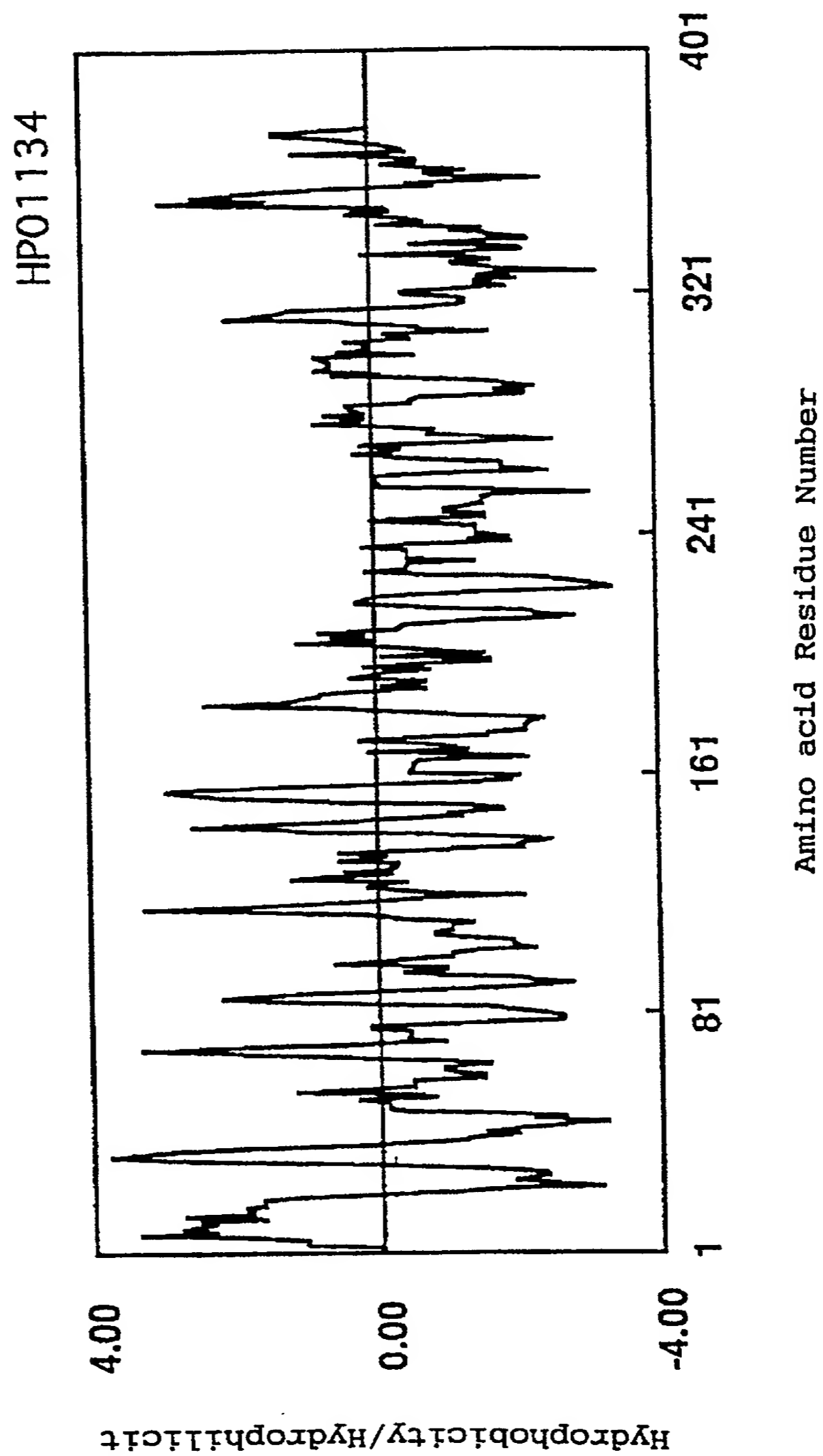


Fig. 5



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Fig. 6



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Fig. 7

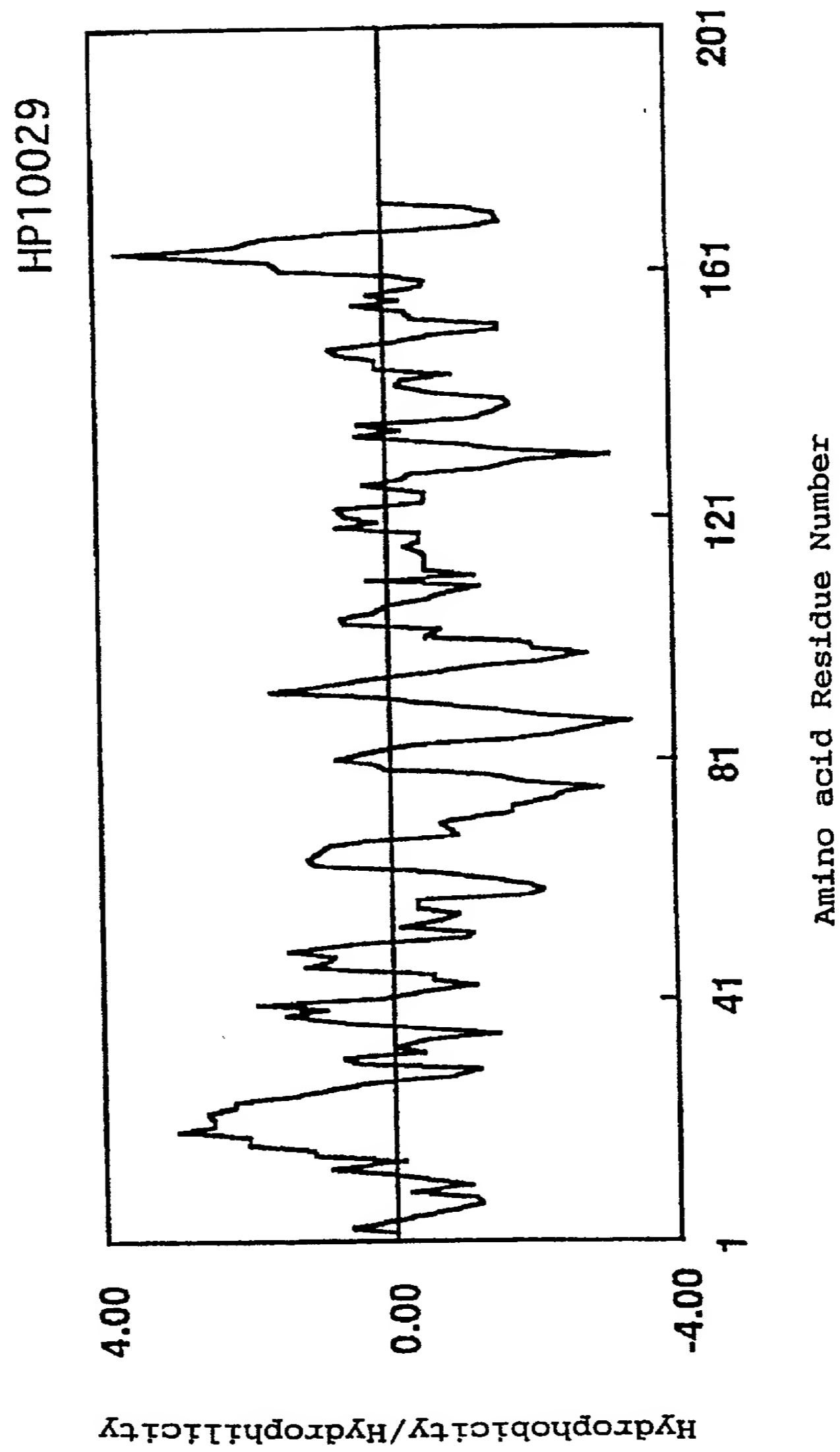
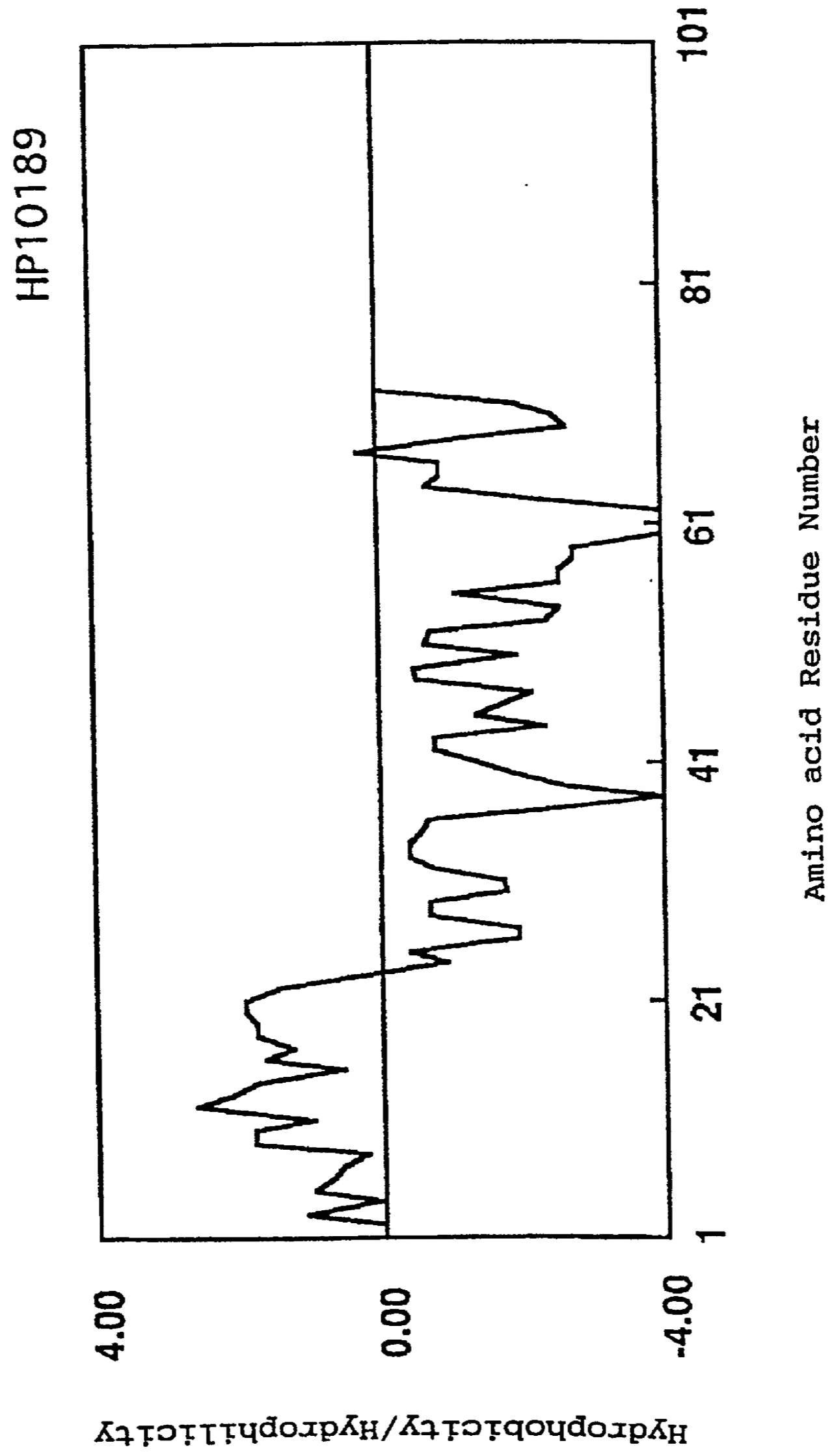


Fig. 8



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Fig. 9

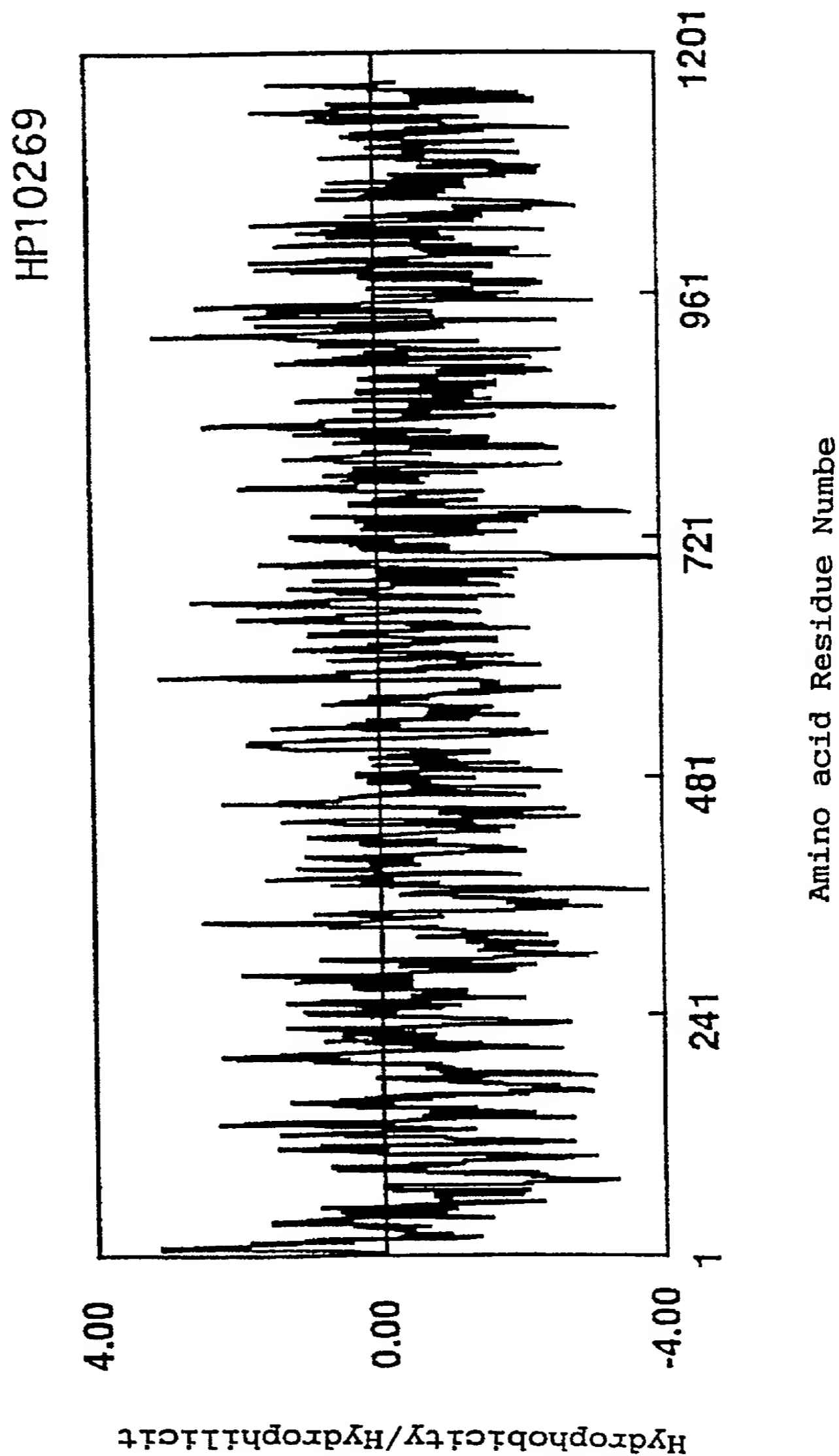


Fig. 10

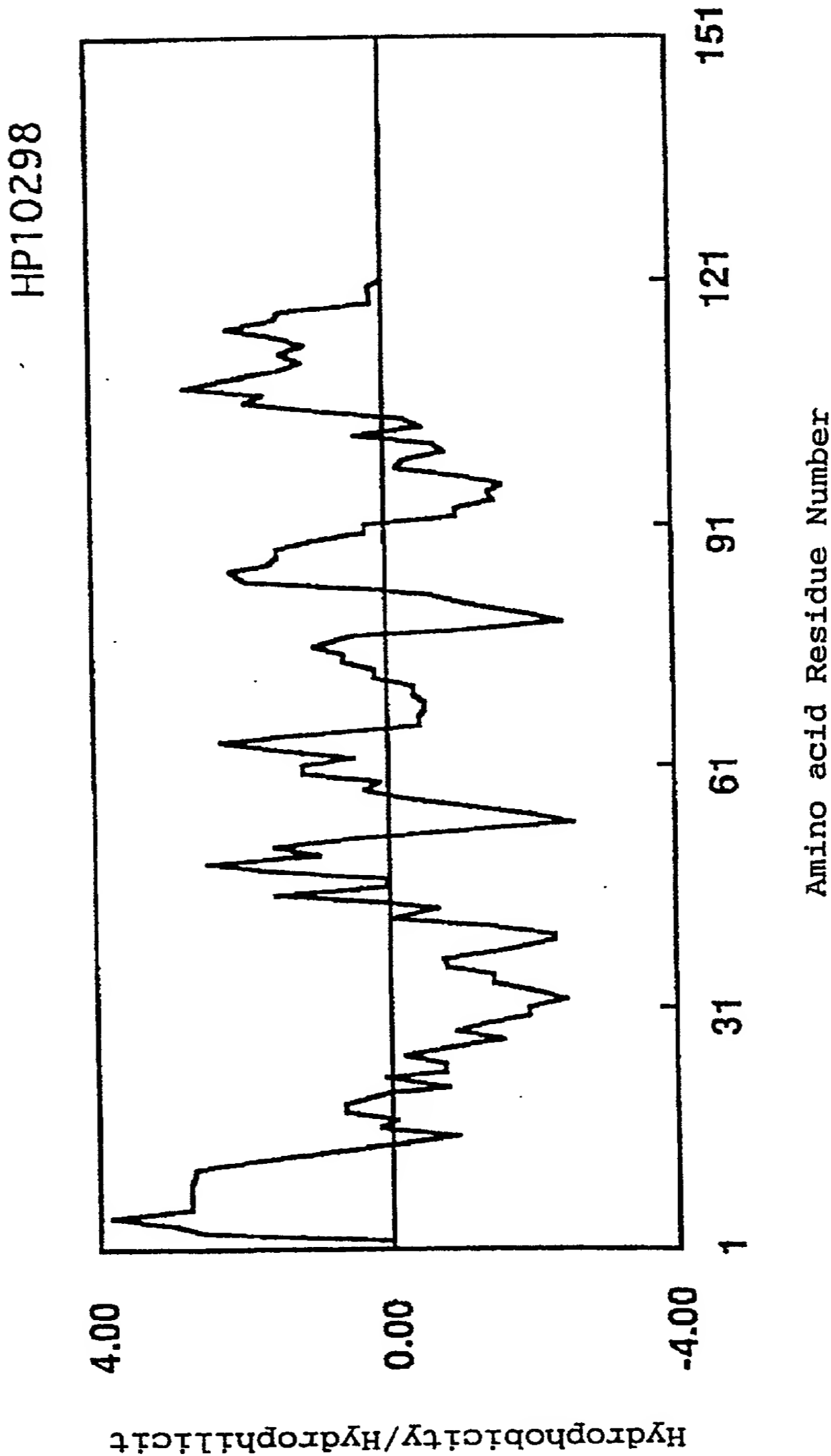


fig.11

